

Socioeconomic burden of moderate and severe Hemophilia A and B in Spain, Real-world evidence insights from the CHESS II Study

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INTRODUCTION

- Hemophilia is a congenital disorder characterized by deficiency or absence of clotting factor VIII in hemophilia A (HA) or factor IX in hemophilia B (HB), resulting in frequent, repeated, and prolonged spontaneous or traumatic bleeding events into joints or soft tissue<sup>1</sup>. The condition severity is classified by the patient's baseline level of factor activity as mild (>5-40%), moderate (1-5%), or severe (<1%)<sup>2,3</sup>. In Spain, there is limited information on the societal economic burden of disease.

OBJECTIVES

To estimate the economic and humanistic burden of disease in adult patients with non-inhibitor moderate and severe HA and HB in Spain.

METHODS

Study Design

- Data for this analysis was drawn from the CHESS II study, a cross-sectional, retrospective, burden of illness study of 1,337 adult males (≥18 years) with hereditary HA and HB of any severity from eight European countries (Spain, France, Germany, Italy, United Kingdom, Denmark, Netherlands and, Romania), and data was collected between November 2018 and October 2020.<sup>4</sup>
- The design and methodology of the CHESS II study have been described in previous publications.<sup>5,6</sup>

Patient Characteristics and Clinical Outcomes

- Patient demographics, clinical characteristics, treatment patterns and outcomes were abstracted from the patients’ medical history by their treating physician, while socioeconomic characteristics (such as workforce participation, non-medical direct costs, indirect costs and health-related quality of life (HRQoL)) were obtained from a voluntary patient self-completed questionnaire (Table 1).
- The main clinical outcomes included annual bleeding rate (ABR), target joints, Problem joints, level of chronic pain, hospital admissions and joint surgeries (Table 2).

Healthcare Resource Use and Costs

- Economic outcomes included direct (medical and non-medical) and indirect hemophilia-related costs in the 12 months prior to data collection. Direct medical costs were obtained from physician. Direct non-medical and indirect costs, resource consumption was obtained from the patient sample.
- Direct and indirect costs were calculated by first taking the mean of the resource and then multiplying that mean by the source unit cost of the resource used during a year. Unit costs (€, 2022 values) for CFRT acquisition and resource consumption, were obtained from local sources.<sup>4,5,7-9</sup>

Health-Related Quality of Life

- The assessment of humanistic outcomes was included in the Patient Public Involvement and Engagement (PPIE) and was based on the responses to the EQ-5D-5L (the index score was calculated using the EuroQol value set for Spain).

RESULTS

Table 1. Sociodemographic and clinical characteristics of patients with HA and HB in Spain

- The study included 181 patients with HA (Moderate: 66, Severe: 115) and 107 patients with HB (Moderate: 28, Severe: 79).

Parameters	Hemophilia A (HA)			Hemophilia B (HB)		
	Moderate (n=66)	Severe (n=115)	Moderate and Severe (n=181)	Moderate (n=28)	Severe (n=79)	Moderate and Severe (n=107)
<b>General characteristics, mean (SD)</b>						
Age, years	40.77 (16.08)	40.43 (14.29)	40.55 (14.93)	40.50 (13.40)	40.58 (14.93)	40.56 (14.49)
Weight, kg	74.79 (9.71)	75.6 (9.07)	75.30 (9.29)	77.61 (11.78)	76.1 (10.12)	76.50 (10.54)
Body mass index, kg/m²	24.63 (2.65)	24.88 (2.57)	24.79 (2.60)	24.65 (2.89)	24.73 (3.36)	24.71 (3.23)
<b>Education, n (%)</b>						
No schooling completed	2 (3.03)	NR	2 (1.10)	NR	NR	NR
No college	36 (54.55)	78 (67.83)	114 (62.98)	13 (46.43)	40 (50.63)	53 (49.53)
College or Advanced Degree	20 (30.30)	33 (28.70)	53 (29.28)	11 (39.29)	36 (45.57)	47 (43.93)
Other	8 (12.12)	4 (3.48)	12 (6.63)	4 (14.29)	3 (3.8)	7 (6.54)
<b>Home circumstances, n (%)</b>						
Lives alone	13 (19.70)	18 (15.65)	31 (17.13)	6 (21.43)	8 (10.13)	14 (13.08)
Lives with family/friends	36 (54.55)	78 (67.83)	114 (62.98)	13 (46.43)	40 (50.63)	53 (49.53)
Lives with partner	8 (12.12)	19 (16.52)	27 (14.92)	8 (28.57)	21 (26.58)	29 (27.10)
Nursing home	NR	NR	NR	1 (3.57)	1 (1.27)	2 (1.87)
Don't know/other	9 (13.64)	4 (3.48)	13 (7.18)	6 (21.43)	5 (6.33)	11 (10.28)
<b>Comorbidities, n (%)</b>						
Anemia	6 (9.09)	12 (10.43)	18 (9.94)	3 (10.71)	8 (10.13)	11 (10.28)
Anxiety	10 (15.15)	26 (22.61)	45 (24.86)	1 (3.57)	16 (20.25)	17 (15.89)
<b>Treatment strategy, n (%)</b>						
No treatment received in the 12 months prior <sup>a</sup>	41 (62.12)	NR	41 (22.65)	21 (75.00)	NR	21 (19.63)
Primary prophylaxis	NR	22 (19.13)	22 (12.15)	NR	48 (60.76)	48 (44.86)
Secondary prophylaxis	NR	36 (31.30)	36 (19.89)	NR	11 (13.92)	11 (10.28)
Primary on-demand	20 (30.30)	49 (42.61)	69 (38.12)	6 (21.43)	18 (22.78)	24 (22.43)
Secondary on-demand	5 (7.58)	8 (6.96)	13 (7.18)	1 (3.57)	2 (2.53)	3 (2.80)
<b>Treatment class, n (%)</b>						
EHL	4 (6.06)	16 (13.91)	20 (11.05)	1 (3.57)	23 (29.11)	24 (22.43)
Plasma-derived	2 (3.03)	16 (13.91)	18 (9.94)	2 (7.14)	30 (37.94)	32 (29.91)
SHL	58 (87.87)	82 (71.30)	140 (77.35)	25 (89.29)	26 (32.91)	51 (47.66)

Abbreviations: EHL: Extended half-life; NR: None reported; SD: Standard deviation; SHL: Standard half-life.

a. Part-time employed < 30 hours per week.

b. No treatment was reported/needed in the 12 months immediately preceding data collection.

Table 2. Clinical outcomes of patients with HA and HB in Spain

- A higher mean (SD) ABR was observed in severe [HA 4.36 (9.38); HB 4.57 (6.44)] compared to moderate [HA 2.77 (3.57); HB 3.64 (4.27)] hemophilia.

Parameters	Hemophilia A (HA)			Hemophilia B (HB)		
	Moderate (n=66)	Severe (n=115)	Moderate and Severe (n=181)	Moderate (n=28)	Severe (n=79)	Moderate and Severe (n=107)
<b>Bleeding outcomes</b>						
ABR, mean (SD)	2.77 (3.57)	4.36 (9.38)	3.78 (7.80)	3.64 (4.27)	4.57 (6.44)	4.33 (5.94)
<b>Cause of bleeding (proportion), % (SD)</b>						
Trauma-related bleeding events	59.14 (29.43)	58.70 (29.52)	58.86 (29.41)	67.86 (29.48)	60.03 (27.93)	62.11 (28.42)
Spontaneous bleeding events	40.86 (29.43)	41.30 (29.52)	41.14 (29.41)	32.14 (29.48)	39.97 (27.93)	37.89 (28.42)
Target joints, n (%) <sup>a</sup>	23 (34.85)	61 (53.04)	84 (46.41)	9 (32.14)	20 (25.32)	29 (27.10)
<b>Problem Joints, n (%)<sup>b</sup></b>						
	31 (46.97)	55 (47.83)	86 (47.51)	8 (28.57)	38 (48.10)	46 (42.99)
<b>Joint procedures (in prior 12 months), n (%)</b>						
	10 (15.15)	29 (25.22)	39 (21.55)	1 (3.57)	5 (6.33)	6 (5.61)
<b>Surgical intervention type, n (%)</b>						
Arthrocentesis	9 (13.64)	24 (20.87)	33 (18.23)	NR	6 (7.59)	6 (5.61)
Arthroscopy	6 (9.09)	9 (7.83)	15 (8.29)	NR	3 (3.80)	3 (2.80)
Arthrodesis	2 (3.03)	5 (4.35)	7 (3.87)	NR	NR	NR
Synovectomy	1 (1.52)	3 (2.61)	4 (2.21)	1 (3.57)	2 (2.53)	3 (2.80)
Arthroplasty	2 (3.03)	2 (1.74)	4 (2.21)	NR	1 (1.27)	1 (0.93)
<b>Number of joint procedures, mean (SD; n)</b>						
Nº of joint procedures in the total sample	0.58 (2.17; 66)	0.63 (1.76; 115)	0.61 (1.91; 181)	0.04 (0.19; 28)	0.15 (0.46; 79)	0.12 (0.41; 107)
<b>Hospital admissions, mean (SD; n)</b>						
Nº of occurrences in the total sample	0.61 (0.70; 66)	0.72 (1.03; 115)	0.68 (0.92; 181)	0.50 (0.81; 28)	1.11 (0.81; 79)	0.89 (0.86; 107)
<b>Related to joint procedures<sup>c</sup></b>						
Nº occurrences in the total sample	0.36 (1.35; 66)	0.39 (1.01; 115)	0.38 (1.14; 181)	0.04 (0.19; 28)	0.14 (0.42; 79)	0.11 (0.37; 107)
<b>Chronic pain level related to hemophilia, n (%)</b>						
No pain	18 (27.27)	33 (28.70)	51 (28.18)	10 (35.71)	8 (10.13)	18 (16.82)
Mild pain	24 (36.36)	34 (29.57)	58 (32.04)	11 (39.29)	40 (50.63)	51 (47.66)
Moderate pain	22 (33.33)	36 (31.30)	60 (33.15)	7 (25.00)	26 (32.91)	33 (30.84)
Severe pain	2 (3.03)	10 (8.70)	12 (6.63)	NR	5 (6.33)	5 (4.67)

Abbreviations: ABR: Annual bleed rate; n: International unit; NA: Not available due to sample size; NR: None reported; SD: Standard deviation.

a. Proportion of the sample that had at least one target joint.

b. Proportion of the sample that had a surgical intervention in their joints in the past 12 months.

c. Number of times a patient has required ward hospitalization (at least one night) due to a bleeding event.

d. Number of times a patient has required ward hospitalization (at least one night) due to a joint procedure.

- Patients with severe HA presented a higher mean number of specialist consultations than patients with moderate HA during the 12 months.
- The mean annual consumption of EHL-CFRT per patient was estimated at 19,800 IU (moderate HA), 315,886 IU (severe HA), 192,000 IU (moderate HB) and 389,080 IU (severe HB). The mean annual consumption of SHL-CFRT per patient was estimated at 10,821 IU (moderate HA), 202,460 IU (severe HA), 2,700 IU (moderate HB) and 257,108 IU (severe HB) (Table 3).

Table 3. Resource use and direct cost components for patients with HA and HB in Spain

	Hemophilia A (HA)		Moderate and Severe (n=181)	Hemophilia B (HB)		Moderate and Severe (n=107)
	Moderate (n=66)	Severe (n=115)		Moderate (n=28)	Severe (n=79)	
Specialist consultations per patient in the past 12 months, mean (SD)						
Treating hematologist visits	8.73 (8.67)	10.26 (7.59)	9.70 (8.01)	8.61 (9.94)	7.48 (5.29)	7.78 (6.78)
Nurse specialist visits	8.20 (10.20)	9.90 (11.15)	9.28 (10.82)	8.36 (10.38)	10.82 (21.32)	10.18 (19.06)
Lab tests per patient in the past 12 months, mean (SD)						
Biochemistry blood test	5.52 (4.43)	5.80 (4.38)	5.70 (4.39)	6.52 (7.08)	4.85 (3.32)	5.51 (4.57)
Coagulation test	5.92 (4.50)	6.03 (4.33)	5.99 (4.37)	8.27 (8.28)	5.47 (3.44)	6.61 (5.12)
Hemoglobin	5.82 (4.64)	6.18 (4.41)	6.05 (4.47)	6.50 (5.79)	5.49 (3.31)	5.86 (4.08)
Hemophilia-related hospitalizations, mean (SD)						
	0.86 (1.20)	0.97 (1.23)	0.93 (1.22)	0.79 (1.17)	0.80 (1.32)	0.79 (1.28)
Bleed-related (in patients with ≥1), mean (SD; n)						
Day cases, N° occurrences	1.00 (0.00; 4)	1.00 (0.00; 3)	1.00 (0.00; 7)	1.33 (0.58; 3)	1.13 (0.35; 8)	1.18 (0.40; 11)
Ward stay, LOS (days)	4.76 (2.72; 29)	6.24 (4.64; 45)	5.66 (4.04; 74)	6.86 (4.10; 7)	5.46 (7.69; 28)	5.74 (7.09; 35)
ICU stay, LOS (days)	1.33 (0.58; 3)	1.90 (0.99; 10)	1.77 (0.93; 13)	NR	1.00 (0.00; 2)	1.00 (0.00; 2)
Joint surgery-related (in patients with ≥1), mean (SD; n)						
Day cases, N° occurrences	1.33 (0.58; 3)	1.44 (1.01; 9)	1.42 (0.90; 12)	NR	1.00 (NA; 1)	1.00 (NA; 1)
Ward stay, LOS (days)	5.56 (5.22; 9)	5.58 (8.43; 24)	5.58 (7.61; 33)	3.00 (NA; 1)	6.33 (6.95; 9)	6.00 (6.63; 10)
Joint surgeries, mean (SD)						
Arthrocentesis	0.29 (0.92)	0.38 (0.91)	0.35 (0.92)	NR	0.08 (0.27)	0.06 (0.23)
Arthrodesis	0.05 (0.27)	0.07 (0.41)	0.06 (0.37)	NR	NR	NR
Arthroplasty	0.03 (0.17)	0.02 (0.13)	0.02 (0.15)	NR	0.01 (0.11)	0.01 (0.10)
Arthroscopy	0.17 (0.78)	0.09 (0.31)	0.12 (0.53)	NR	0.04 (0.19)	0.03 (0.17)
Synovectomy	0.05 (0.37)	0.07 (0.57)	0.06 (0.51)	0.04 (0.19)	0.03 (0.16)	0.03 (0.17)
CFRT per treatment class in IU, mean (SD)						
EHL	19,800 (14,033)	315,886 (284,559)	263,635 (281,696)	192,000 (NA)	389,080 (627,036)	380,511 (613,956)
Plasma-derived	92,100 (124,309)	173,467 (321,100)	163,894 (303,172)	10,734 (1,604)	365,173 (397,331)	341,544 (393,790)
SHL	10,821 (37,533)	202,460 (322,190)	120,126 (261,804)	2,700 (9,991)	257,108 (193,554)	134,992 (188,800)
All-class mean	13,828 (41,935)	213,338 (317,214)	138,964 (270,003)	10,306 (37,571)	335,124 (427,448)	249,977 (394,098)

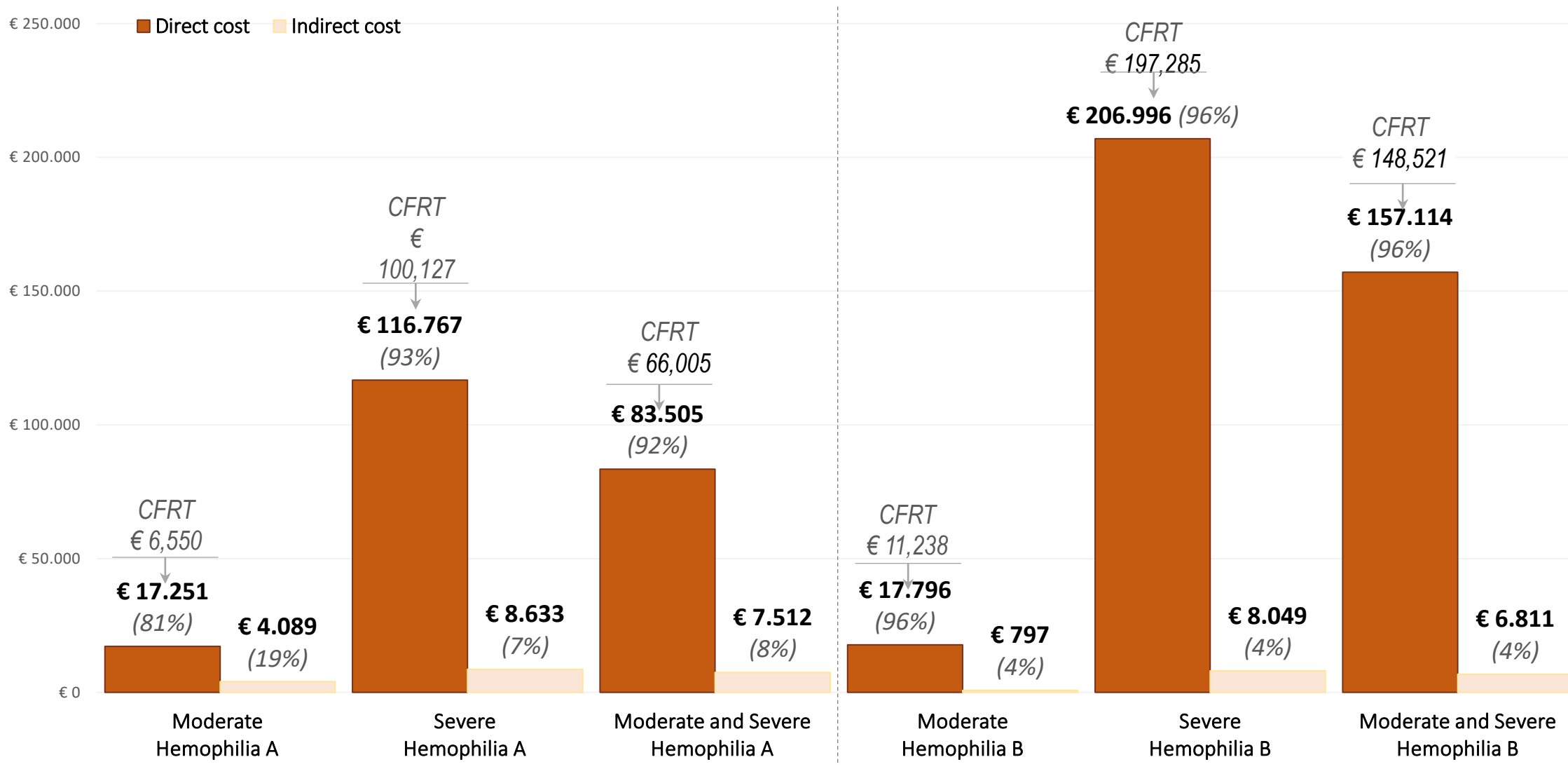
Abbreviations: EHL: Extended half-life; NA: not available due to sample size; NR: None reported; LOS: Length of stay; SD: Standard deviation; SHL: Standard half-life.

- The mean (SD) requirement for informal care was 7.84 (7.78) hours per week for patients with moderate or severe HA (n=38) and 13.61 (9.86) for patients with moderate or severe H B (n=18), respectively.
- The mean (SD) EQ-5D-5L score reported by Spanish patients was 0.81 (0.15) for moderate HA, 0.77 (0.18) for severe HA, 0.86 (0.17) for moderate HB and 0.70 (0.22) for severe HB.

Total Costs

- The economic burden increased substantially with increasing severity (Figure 1). The mean annual per-patient direct cost ranged from €17,251 (moderate HA) to €206,996 (severe HB), in which CFRT consumption represents between 38% (moderate HA) and 95% (severe HB) of the direct cost. The mean annual per-patient indirect cost ranged from €4,089 (moderate HA) to €8,049 (severe HB). The total annual per-patient cost (direct and indirect cost) was €21,340 for patients with moderate and severe HA, respectively; while in HB it ranged from €18,592 to €215,045 for moderate and severe condition, respectively. The average annual per-patient cost for HA and HB was €91,017 and €163,925, respectively.

Figure 1. Annual Direct and Indirect cost per patient with HA and HB in Spain



CONCLUSIONS

This is the first descriptive analysis to provide information related to the economic and humanistic burden of adult patients with moderate and severe HA and HB in Spain, without inhibitor diagnosis. The results of this analysis suggest that, regardless of hemophilia type, increased disease severity was associated with increased costs and decreased patient-reported HRQoL.

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DISCLOSURE

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