Lifetime Economic Burden of Hemophilia Using Phase-Based Costing and Survival Estimation Through Rolling Extrapolation

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Background & Aim

- Hemophilia treatment is initiated at an early age and continued for a lifetime.
- Recurrent joint bleeding causes an irreversible joint damage, known as hemophilic arthropathy which poses clinical and economic burden on the patients.
- There is not enough evidence about the lifetime economic burden of hemophilia which considers worsened economic burden due to disease progression and age.
- We aim to identify the real-world lifetime cost of hemophilia, considering cost changes by disease phase and time.

Methods

Data Source

- 2007-2022 Health Insurance Review and Assessment (HIRA) database of South Korea

Study Population

- Male patients with hemophilia A (ICD10: D66) or Hemophilia B (ICD10: D67) between 2007-2022

Outcome measures

- **Survival estimation**
  - **Rolling Extrapolation**: Predict survival probability beyond observation using the relative survival function between hemophilia patients and the general population
  - **Life expectancies**: calculated using the width of the area under the estimated survival curves
- **Phase-specific costing**
  - **3 phases**: (1) before hemophilic arthropathy, (2) after hemophilic arthropathy, (3) before death (from 1 year before death to death)
- **Incidence rate (IR) of hemophilic arthropathy**
  - calculated with time from the first diagnosis of hemophilia to the first incidence of hemophilic arthropathy (ICD10: M362).
  - used the IR to calculate the transition probability from 'before hemophilic arthropathy' to 'after hemophilic arthropathy,' with $p(t) = 1 - e^{-rt}$, where p is probability, r is incidence rate, and t is cycle length (1 year in our study)
- **Phase-specific cost prediction**
  - The annualized phase-specific cost data were used to fit generalized estimating equations (GEEs) to estimate phase-specific annual costs before and after the observed period.
- **Lifetime Costs**
  - Hypothetical patients: born in 1990, 2000, and 2010
  - It was assumed that hemophilia treatment is continued for a lifetime horizon.
  - Lifetime costs were calculated by summing the annual treatment costs to the estimated life expectancy, which was calculated by multiplying the estimated probability of each phase by the corresponding phase-specific annual cost.

Conclusions

Implications

- Considering the average lifetime healthcare cost per capita in South Korea, which was $92,340 in 2012, the lifetime economic burden posed by hemophilia is substantial, with approximately 136 and 240 times the average lifetime health expenditure per capita in South Korea for hemophilia B and A, respectively.
- Unlike previous studies of lifetime-horizon cost of hemophilia which applied only a discount rate for future costs, we reflected the changing trend in phase-specific annual costs over time, leading to more realistic results.
- Higher price of coagulation factor used for hemophilia B than A in South Korea could have contributed to the higher cost of hemophilia B. Moreover, an extended length of stay or suboptimal use of coagulation factors could have contributed to the higher cost of hemophilia B.

Limitations

- Our results may not be generalizable to other countries or perspectives. However, the comparisons between hemophilia types, different phases, and trends in costs over time could be informative for researchers outside South Korea.
- The phases were not defined according to hemophilia severity, which is classified with the blood clotting factor levels in our study. However, because the onset of hemophilic arthropathy indicates symptom deterioration, irreversible damage, and a significant economic burden on patients, hemophilic arthropathy was deemed appropriate for use in phase-specific cost estimation.
- Our cost estimation does not account for unexpected cost escalations or reductions from unpredictable events, such as pandemics or drug development.
- We assumed a consistent incidence rate of hemophilic arthropathy across different ages owing to a lack of data on age-specific incidence rates.

Conclusions

- Hemophilia imposes a considerable lifetime economic burden, being higher for Hb than Ha. Estimated real-world lifetime burden of hemophilia could assure adequate resource allocation for hemophilia treatment.

References

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Abbreviations: CI, confidence interval; GEE, generalized estimating equation; ICD, international statistical classification of disease; IQR, interquartile range; SD, standard deviation

Results

- In total, 2,624 male patients with hemophilia A and 664 male patients with hemophilia B were included (**Table 1**). Patient characteristics were not significantly different between the hemophilia A and B groups.
- Over 70% of patients experienced incident hemophilic arthropathy during the observation period.
- The proportion of patients who died during the observation period was 7.47% and 5.72% in the hemophilia A and B groups, respectively.

Table 1. Baseline characteristics of the included patients

	Hemophilia A	Hemophilia B	p-value
Total population 2007-2022, n	2,624	664	
Hemophilic Arthropathy, n (%)	1,932 (73.63)	469 (70.63)	0.1203
Observed period, days			0.2357
Mean (SD)	4,513 (1,761)	4,423 (1,742)	
Median (IQR)	5,661 (3,310-5,801)	5,425 (3,097-5,794)	
Death, n (%)	196 (7.47)	38 (5.72)	0.1179
Prevalent patients in 2022, n	2,435	628	
Age of prevalent patients in 2022			0.9754
Mean (SD)	34 (18)	34 (19)	
Median (IQR)	32 (21-47)	32 (17-47)	

- With an incidence rate of hemophilic arthropathy (Hemophilia A: 0.090 case/person-year [95% CI, 0.084-0.097]; Hemophilia B: 0.080 [0.070-0.092]), the annual transition probability from 'before hemophilic arthropathy' to 'after hemophilic arthropathy' was estimated at 0.086 (Hemophilia A) and 0.077 (Hemophilia B).
- The estimated life expectancy was 76.13 (Hemophilia A) and 77.54 years (Hemophilia B). Compared to the general population, the loss of life expectancy was 3.46 (Hemophilia A) and 2.06 years (Hemophilia B) (**figure 1**).

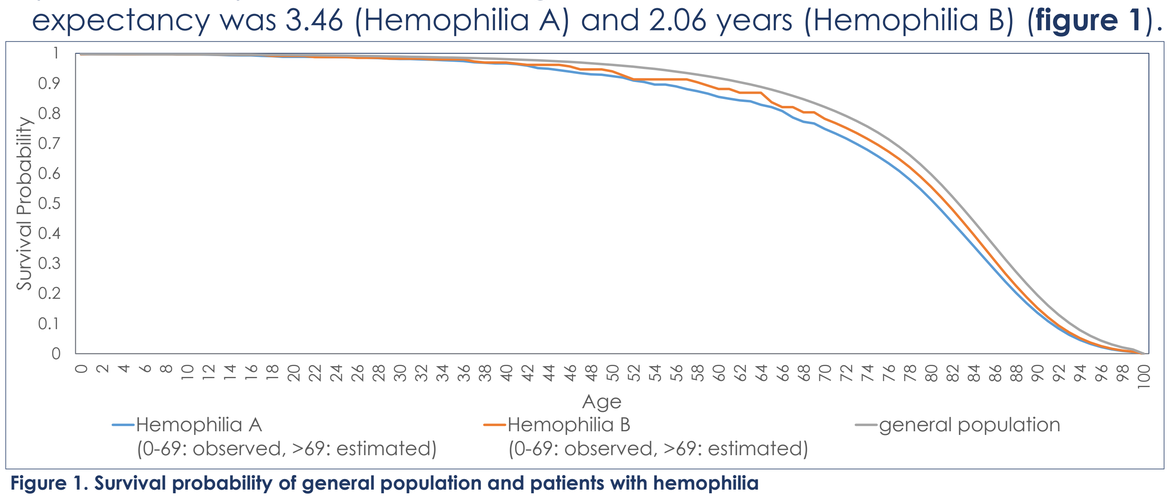

Figure 1. Survival probability of general population and patients with hemophilia

- The phase-specific annual cost of 'before hemophilic arthropathy' and 'after hemophilic arthropathy' was significantly higher in hemophilia B, showing 1.3 to 1.4 times higher costs compared to hemophilia A ($p<0.05$) (**figure 2**).

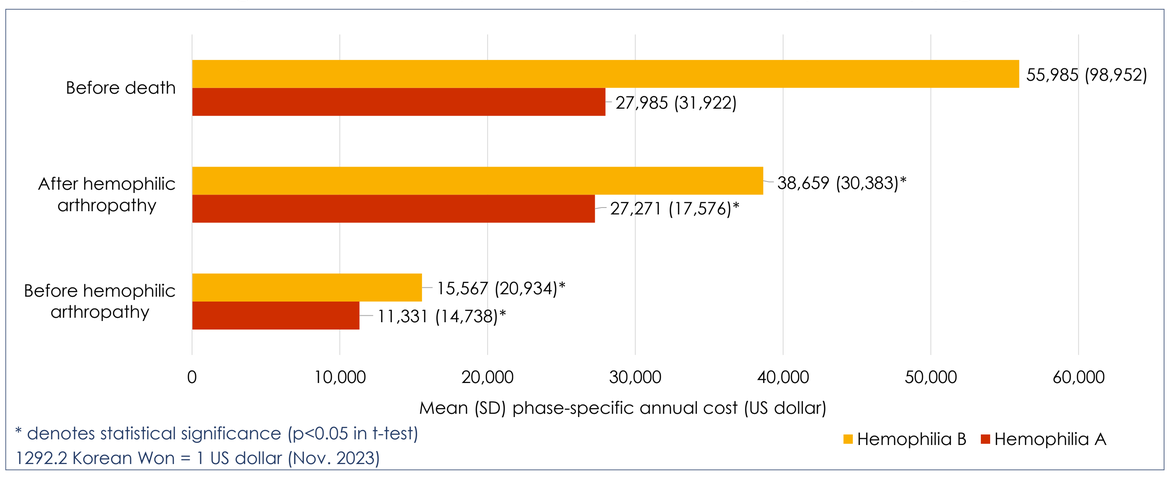

Figure 2. Phase-specific annual cost of hemophilia

- Using the estimates from GEEs, lifetime costs of Hemophilia A were $7,068,429 for hypothetical patients born in 1990 and increased to $12,624,218 and $22,553,959 for hypothetical patients born in 2000 and 2010, respectively. For hemophilia B, lifetime costs calculated with the GEE estimates were $11,963,026, $22,250,382, and $41,410,833 for hypothetical patients born in 1990, 2000, and 2010, respectively.
- Lifetime cost was 1.69-1.84 times higher in Hemophilia B than Hemophilia A (**figure 3**).

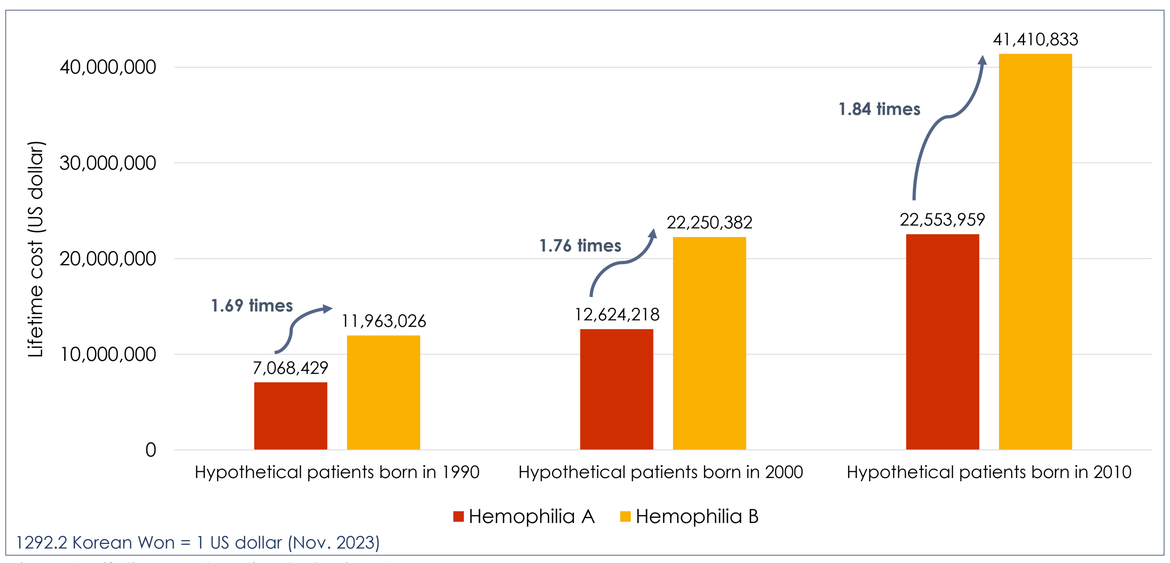

Figure 3. Lifetime costs estimated using GEE