Economic Burden of Hemophilia B in the US: A Systematic Literature Review

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INTRODUCTION

- Hemophilia B (HB) is a rare disease caused by congenital Factor IX (FIX) deficiency. HB requires life-long management to prevent or manage bleeding and associated morbidity.
- Although HB affects only a small portion of the population, it is associated with high overall cost and imposes a significant financial burden on individuals, payers, and society in general.
- Due to variation in patient clinical characteristics and treatment choice, cost and healthcare resource utilization associated with disease management can vary significantly from patient to patient. Also, type of the clotting factor in use: standard half-life (SHL) vs extended half-life (EHL) greatly impact associated costs.

OBJECTIVE

- The literature review was conducted to identify studies describing costs and resource utilization associated with HB in the US.

METHODS

- A systematic literature review was performed by searching relevant electronic databases (MEDLINE and Tufts Cost-Effectiveness Analysis Registry) to identify full-text studies (search period: 03/2009-03/2019). Additionally, a manual search for abstracts from relevant conferences was performed (search period: 01/2016-03/2019).
- Studies were included in the review using predefined criteria with respect to: population (HB) and study type (budget impact model, cost study, burden of illness study, healthcare resource utilization study or economic evaluation).
- Two reviewers, working independently, reviewed titles and abstracts from the literature searches and selected potentially relevant studies according to the inclusion and exclusion criteria. Disagreements were resolved by discussion between reviewers.
- Outputs presented for different time periods like: per patient per month (PPPM) or per patient per quarter (PPPQ), 5 years, lifetime, and others were adjusted to annual cost\resource use per patient per year (annual PP).
- Only results which could be presented as per-patient mean/median values were included.

RESULTS

Study characteristics

- 693 titles and abstracts were screened. A total of 17 studies evaluating cost and resource utilization in patients with HB in the US were included.
- Of the included studies: 10 investigated the cost/resource use of HB patients only, and 7 studied patients with hemophilia A and B with results presented by each subtype separately.
- Most studies (94%) reported cost from the healthcare payer perspective. The societal perspective (formed of both direct and indirect cost) was reported in only a single study.
- Included studies predominantly analyzed insurance claims databases, followed by the analysis of medical records.
- Three main cost categories were identified across all studies: direct medical cost, direct non-medical cost, and indirect cost.

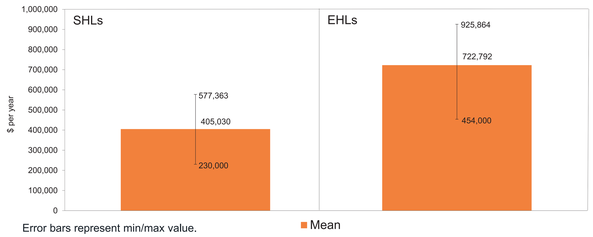
Total direct medical cost

- Three studies presented total direct medical cost of HB management. Median cost ranged from $23,256 (Armstrong et al. 2014 [10]), through $51,814 (Chen CX et al. 2017 [3]), to $311,928 for patients on SHLs and $738,728 for patients on EHLs (Chhabra et al. 2017 [7]).
- Reported cost of FIX therapy constituted over 98% of total annual medical cost regardless of factor type (SHL/EHL) (Chen CX et al. 2017 [3], Chhabra et al. 2017 [7]).
- Variation in cost across studies could be due to disease severity (severe, moderate, and mild), treatment regimen (prophylaxis and on-demand), and other factors.

Clotting factor cost

- **Figure 1** presents mean annual cost of FIX therapy for HB with respect to clotting factor half-life (based on 8 studies; means calculated irrespective of disease severity or treatment regime). Mean annual factor cost for SHL products was around 44% lower from EHL FIX treatment ($405,030 vs $722,792).

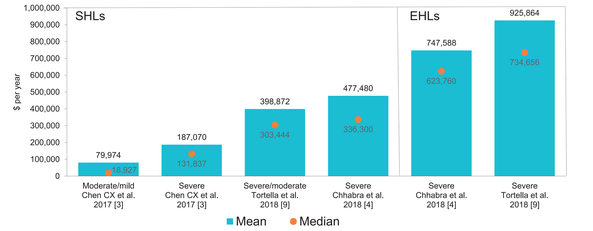
Figure 1. Annual PP clotting factor cost (SHLs vs EHLs)



Error bars represent min/max value.

- Irrespective of the type of FIX therapy, patients with severe disease reported higher cost than patients with moderate or mild disease. **(Figure 2)**.

Figure 2. Annual clotting factor cost PP with respect to FIX type and disease severity



Clotting factor utilization

- Factor utilization was found to depend on the factor type **(Figure 3, Figure 4)**. Annual FIX consumption was lower in patients receiving EHL versus SHL therapy. The mean annual utilization of SHLs amounted to 313,717 IU versus 232,708 IU in EHLs.

Figure 3. Annual PP utilization of SHLs (IUs)

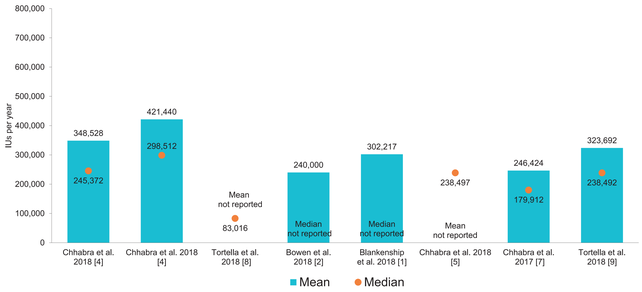
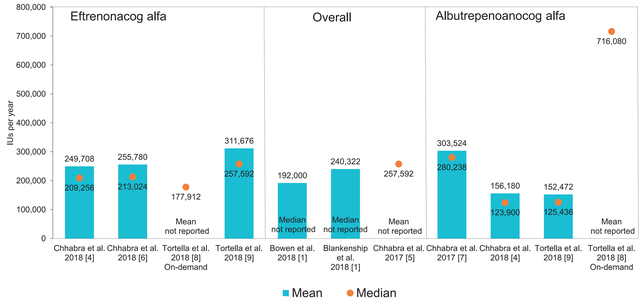


Figure 4. Annual PP utilization of EHLs (IUs)



DISCUSSION

- Clotting factor cost constituted the majority of total cost for HB management (over 98%), regardless of hemophilia subtype, treatment strategy or factor type.
- Prophylaxis versus on-demand treatment substantially increased the direct costs of HB management, presumably due to increased factor replacement costs.
- Patients with severe HB reported higher costs for replacement therapy compared with a moderate or mild cohort.
- Mean annual factor cost for SHL therapy was around 44% lower from FIX EHL treatment ($405,030 vs $722,792).
- Underlying differences in patients' clinical profiles may influence the required treatment regimen, therefore differences in clinical factors between SHL/EHL groups could account for some of the difference in factor consumption.
- Expected rise in the number of HB patients switching from SHL to EHL could generate substantial burden to the payers for routine FIX prophylaxis.

LIMITATIONS

- Differences in the methodological approach in terms of cost aggregation (including differences in the way costs were defined by individual studies) restricted comparison of results across studies.
- Additionally, different data sources were used when collecting information on costs and resource use. Although most of the studies relied on data claims as a primary source of data, information for different time periods were analyzed.
- Majority of studies were based on insurance claims databases. These data have limited information about patients' clinical characteristics, what can be significant obstacle for cross-sectional analysis of observed differences in costs among included studies.

CONCLUSION

- **This systematic literature review found substantial economic burden associated with HB in the US. Mean annual clotting factor cost of HB management was found to range from $230,000 to $577,363 for a patient on SHL treatment and from $454,000 to $925,864 for those on EHLs.**
- **The significant costs and health resources utilized by patients highlight unmet medical needs remaining in HB management.**

ACKNOWLEDGEMENT

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REFERENCES

1. Blankenship et al. Change in factor cost s and units consumption by people with hemophilia A and B after switching from a standard half-life product to extended half-life product. In: NHF 2018, Orlando, US.
2. Bowen et al. Incremental Cost of Switching to Extended-Half-life (EHL) Coagulation Factor Products to Treat Hemophilia Among 15 Million Commercially Insured Members. In: AMCP 2018, Boston, US.
3. Chen CX et al. Economic Burden of Illness among Persons with Hemophilia B from HUGS Vb: Examining the Association of Severity and Treatment Regimens with Costs and Annual Bleed Rates. Value Heal. 2017;2008:1074-1082.
4. Chhabra et al. Real-world data analysis of us claims data on coagulation factor ix dispensation and expenditures in patients with severe hemophilia B: standard half-life vs. Extended half-life products. In: ISPOR Europe 2018, Barcelona, Spain.
5. Chhabra et al. Real-world health care utilization costs in hemophilia b patients using standard and extended half-life recombinant factor IX products. In: ISPOR 22nd Annual International Meeting 2018, Boston, MA, US.
6. Chhabra et al. Real-World expenditures associated with Prophylactic Factor IX replacement in Severe Hemophilia B patients in the US: A comparison between standard and extended half-life products. In: WFH 2018, Glasgow, Scotland.
7. Chhabra et al. Real-world Health Care Utilization and Costs of Extended and Standard Half-life Recombinant Factor IX Products in Hemophilia B patients. ISTH 2017, Berlin, Germany.
8. Tortella. et al. Comparison of standard half-life to extended half-life fix products: Real- world analysis or recent factor IUS dispensed and expenditure in on- demand hemophilia B patients. In: EAHAD 2018, Madrid, Spain.
9. Tortella et al. Real-World Analysis of Dispensed IUs of Coagulation Factor IX and Resultant Expenditures in Hemophilia B Patients Receiving Standard Half-Life Versus Extended Half-Life Products and Those Switching from Standard Half-Life to Extended Half-Life Products. J Manag Care Spec Pharm. 2018;24(7):643-653.
10. Armstrong et al. Costs and utilization of hemophilia A and B patients with and without inhibitors. J Med Econ. 2014;17(11):798-802.