Economic Burden of Hemophilia

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HEMATOLOGY UTILIZATION GROUP STUDIES

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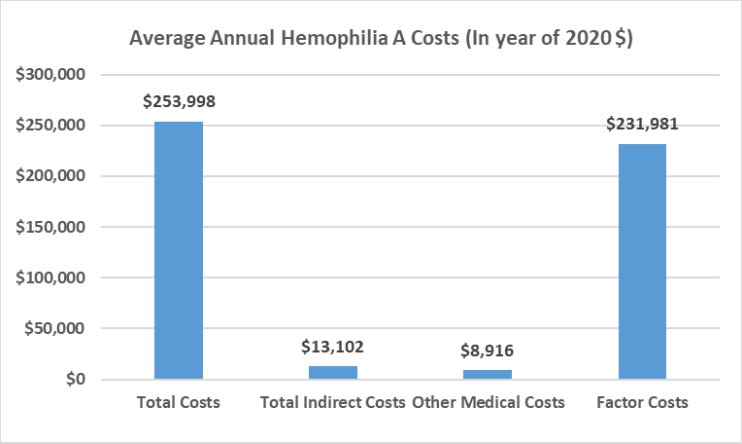
Overview

Hemophilia is a rare, complex, and potentially fatal bleeding disorder. It is currently incurable and often places physical, social and economic strain on affected individuals and their families. Hemophilia is associated with extremely high monetary costs as well as high social costs, such as reduced quality of life and reduced employment and educational achievement. This policy brief focuses on the economic burden of illness associated with hemophilia A (HA) and hemophilia B (HB). Data cited in this brief are taken from samples of affected persons who receive care throughout the United States at federally-supported Hemophilia Treatment Centers (HTCs).

Calculating Cost of Care

Direct and Indirect Costs



Direct costs include tangible items, such as medications, hospitalizations and outpatient visits and are usually calculated from the patient or payor perspective. Indirect costs, often calculated from a societal, individual, or employer perspective, include three potential sources (mortality, absenteeism, and the reduced productivity of employees. (1). Hemophilia costs are driven largely by the cost of medications. (2) When present the cost in 2020 US $, HUGS data indicates that the average annual total costs (direct plus indirect) for people of all ages with hemophiliaA is $253,998. Hemophilia therapies (also known as 'factor concentrates') accounted for 91.3% of total costs, non-factor medical costs for 3.5%, and indirect costs for 5.1%.

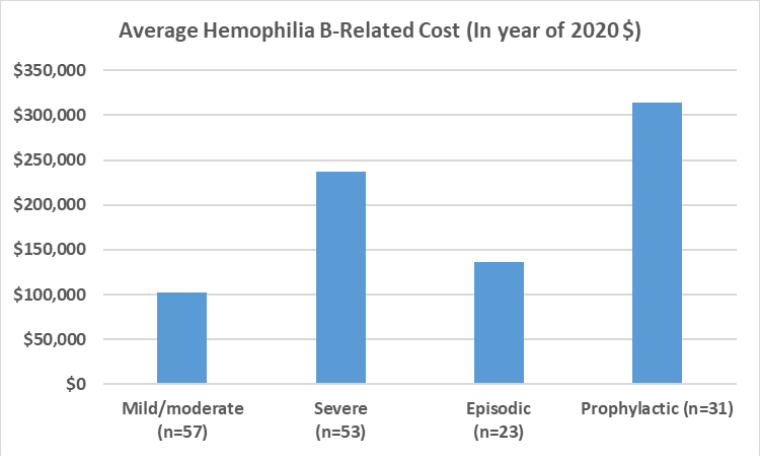
Clinical Characteristics and Costs

Hemophilia severity, treatment regimen and inhibitor status are clinical characteristics that can substantively impact hemophilia cost of care. Obtaining care at federally-supported Hemophilia Treatment Centers, and treating via medically supervised home management reduces costs, as well. (3, 4)

- ## Severity

Severity refers to the amount of clotting protein (FVIII in HA and XI in HB) circulating in the blood, compared to a person with normal coagulation. Bleeding events in persons with severe disease are more frequent, spontaneous, and life-threatening as bleeds may more often occur in the central nervous and GI systems. Inhibitors, the costliest complication, develop in around 30% hemophilia A and up to 5% hemophilia B. Inhibitors are alloantibodies that neutralize clotting factor concentrates and make bleeding events more difficult to treat. The incidence of inhibitors is increased in African Americans and Hispanic patients for reasons not well understood. Consequently, those with frequent and severe bleeding symptoms are more likely to be prescribed and to benefit from a prophylactic treatment regimen. HUGS study data indicated average annual total costs for persons with mild HA of $76,851, compared to $273,684 for those with severe HA (both using on-demand treatment). (2) Among individuals with HB, individuals with severe disease incurred average annual costs of $236,909 , compared to $102,344 to those with mild or moderate disease. (1)

- ## Treatment regimen: Prophylaxis vs. Episodic



Use of factor concentrate is prescribed for one of two treatment regimens: episodic ("on-demand") or prophylactic.

Episodic treatment involves infusing factor concentrate after a bleeding event has occurred. Although episodic treatment resolves bleeds, permanent damage to joints and/or soft tissue may still occur.

Regular prophylactic treatment is the standard of care for hemophilia, and is recommended by the World Federation of Hemophilia and the National Hemophilia Foundation, effectively prevents bleeds. (5, 6). In affluent countries, prophylactic treatment has transformed hemophilia into a manageable disease by preserving joint health, allowing individuals to lead active and normal lives.

The HUGS HB study found that on average, episodic treatment cost $136,587 annually, compared to $313,823 for prophylactic treatment. (1) Individuals on prophylaxis had fewer emergency room visits, shorter hospitalizations and fewer bleeding episodes. Although each prophylactic infusion costs more than episodic infusions, prophylaxis can lower health care costs over a lifetime, by avoiding complications and disability.

- ## Inhibitor development

Development of an inhibitor to FVIII or FIX treatment products can greatly increase the cost of care. Inhibitors are alloantibodies that neutralize clotting factor concentrates and make bleeding events more difficult to treat. Exactly how and why some individuals develop an inhibitor is only partially understood. (7) Patients with inhibitors who fail treatment with immune tolerance induction therapy (ITI), which attempts to induce immunologic tolerance to the inhibitor with frequent, high doses of factor concentrate, are treated for bleeding episodes with bypassing agents (BPAs). These include activated prothrombin complex concentrates (aPCCs) or recombinant activated FVII (rFVIIa). Although prophylaxis with BPAs effectively reduces bleeding episodes, a significant number of bleeds still occur and individual responses to BPAs are

unpredictable, resulting in very high treatment costs and reduced quality of life. The recent development of a new therapeutic agent, emicizumab (discussed more fully later in this brief), has been shown to be much more effective than aPCC and rFVIIa prophylaxis, and also cost-effective for treating bleeds in individuals with inhibitors. (8)

- ### Access to specialty care through Hemophilia Treatment Centers (HTC)

Specialized coordinated, team-based care is available through the US network of more than 140 federally-supported HTCs which serve approximately 70% of affected US residents. (9) HTCs provide the best treatment outcomes by focusing on disease prevention, reducing bleed-related hospitalizations and mortality, enhancing school and work attendance and producing high rates of high school graduation rates. (3, 4, 10) Private and public payors benefit from HTCs' substantial contributions to improved outcomes, longevity and cost reduction for insured members. HTCs save lives, improve the quality and length of life, and reduce costs.

Developments in Hemophilia Treatment

During the last 20 years, clotting factor concentrate use has grown steadily in economically advantaged countries, due to the development of safe, virally inactivated medications and the adoption of prophylaxis protocols. (11) Today newer therapies are available, dramatically changing treatment patterns and the utilization of hemophilia care services.

- ### Individualized Treatment

Personalized hemophilia treatment uses each patient's unique pharmacokinetic (PK) profile to ensure optimum dosing. (Pharmacokinetics is the study of how a person's body metabolizes a factor product over time). Clinical trials of individualized, PK-guided dosing have lowered annual bleeds by reducing overall doses, longer dosing intervals and requiring fewer infusions. (12)

- ### Emicizumab (Hemlibra©) Impact on Inhibitors

Emicizumab (approved in 2017 for prophylactic use in persons with HA with inhibitors, and in 2018 for those without inhibitors) lowers treatment burden as it is a subcutaneous therapeutic vs intravenous administration with factor concentrates, and by reducing the frequency of injection administration to as little as once every four weeks. Although long-term clinical data is not yet available, numerous modeling studies show emicizumab to be less costly and more effective than legacy inhibitor treatment. (8, 13)

- ### Extended Half-life (EHL) factor concentrates

EHL recombinant FVIII and FIX medications are also available in the US. Standard half-life products are infused two to three times per week, while 'extended' half-life products are infused less frequently (every three to five days for FVIII and weekly to a few times per month for FIX). Less frequent infusions can enhance quality of life without increased risk of inhibitor development. However, studies show higher expenditures (51%-122%) for both FVIII and FIX the 'extended' products. (14, 15)

- ### Gene Therapy

Finally, gene therapy (GT), administered just once, offers the possibility of clotting factor protein DNA delivered to patient cells and inducing endogenous factor VIII or FIX synthesis, with hopes to significantly decrease bleeding rate for many

years. GT aims to reduce the use of factor concentrates or other non-factor prophylactic therapies. Cost-effectiveness modelling studies comparing GT to prophylaxis therapy conclude that GT would cost less and be more effective compared with FVIII prophylaxis, while providing a higher health-related quality of life. (16, 17)

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