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Economic impact of hemophilia type A and B in Mexico

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Abstract

Background: *The treatment of hemophilia generates a disproportionally large economic impact relative to its prevalence.* **Objective:** *To determine the economic impact of hemophilia A and B in Mexico in 2011 from the perspective of public health institutions.* **Methods:** *Hemophilia was epidemiologically characterized in Mexico during the year of interest, direct costs (diagnosis, monitoring or follow-up, care of bleeding events, and consumption of hemostatic factors), as well as absenteeism associated with illness (indirect costs) were estimated. Records, surveys and official data were supplemented by expert opinion to assess costs.* **Results:** *The investment in hemostatic factors is the primary source of cost: 68.6 and 74.3% of total investment in hemophilia A and B, respectively. Sensitivity analysis showed that the most decisive variable is the cost of acquisition of hemostatic factors, including bypass agents. The second most important source of cost is the attention to bleeding events, being significantly higher in patients receiving on-demand treatment compared with those receiving prophylaxis.* **Conclusion:** *In Mexico, hemophilia is a condition whose treatment requires a large amount of financial resources associated with the cost of hemostatic factors and care of hemorrhage, the latter being lower in patients on prophylaxis relative to on-demand.* (Gac Med Mex. 2016;152:15-24)
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Introduction

Hemophilia is a disease that significantly affects the quality of life of those who suffer from it and at the same time generates an economic and social impact of disproportionate magnitude in relation to its prevalence[1-3]. Recent studies indicate that the average cost of a patient with hemophilia in the United States of America (USA) amounts nearly USD 150,000 yearly[4,5]. Additionally, the resolution of a bleeding episode in a hemophilia patient has been described to reach a cost ranging from USD 10,000 to USD 40,000[6], whereas in patients with highly responsive inhibitors the cost can reach USD 83,000[7].

Hemmorrhages into joints and muscles can be very painful and weakening. When the bleeding episodes are repeated in a single site, long-term complications can develop, for example, deforming arhtropathy, the treatment of which will probably require joint-replacement surgery[8-10]. Certain bleeding episodes can put the patient's life at risk[11]. A recently published study highlights that in 2007, hemophilia generated 13,418 life years lost due to premature death and 96,677 disability-adjusted life years lost for a total of 110,095 healthy life years (HLY) lost in the USA[12].

Replacement therapy for the hemophilia patient has two modalities: on-demand treatment, which is applied at the patient's home or in a hospital center at the moment the bleed is clinically identified; and prophylactic

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treatment, which consists in regular and scheduled administration of the deficient factor, generally on a long-term basis, in order to prevent hemorrhages and their complications[13]. In some patients, inhibitors can appear (anti-VIII factor [FVIII] or anti-IX factor [FIX] antibodies according to whether the hemophilia is A or B, respectively), which are able to neutralize or inhibit the capability of the replacement factor administered to stop the bleeding[11]. Patients with high-responding inhibitors (> 5 Bethesda units) can receive treatment with bypassing agents: recombinant activated FVIII (rFVIIa) and activated prothtombin complex concentrate (aPCC)[11,13,14].

According to the National Registry of People with Coagulation Disorders, in the year 2011, the Mexican Institute of Social Security (IMSS – *Instituto Mexicano del Seguro Social)* looked after 57% of 5,096 identified patients in Mexico; the Ministry of Health after 23% and the Institute of Security and Social Services for the Workers at the Service of the State (ISSSTE – *Instituto de Seguridad y Servicios Sociales de los Trabajadores del Estado)*, 5%. In 603 patients (12%), this information was not identified[15].

In Mexico there are no nation-wide studies determining the economic burden of hemophilia. This information could contribute to make the allocation of public resources for the care of patients with this condition more efficient. The purpose of this investigation was to estimate the economic impact of hemophilia A and B in Mexico during the year 2011.

Material and methods

A cost-of-illness study was developed following a prevalent approach: total costs associated with the care of patients with hemophilia (type A or B) recorded on the 2009-2011 Statistical Report of the Hemophilia Federation of the Mexican Republic (FHRM – *Federación de Hemofilia de la República Mexicana)* were estimated[15]. The time horizon for the study was the period encompassed from January 1 to December 31, 2011. That year was selected because it was the most recent for which there was complete information available on all parameters included in the analysis. The direct medical costs estimation was developed from the perspective of the public institutions of the National Health System in Mexico. The unit cost of health resources used in the management of hemophilia was obtained from different institutional sources, especially from the IMSS.

The consumption of institutional resources was estimated based on the opinion of 8 clinical experts on hemophilia, all of them specialists of recognized institutional trajectories (at the IMSS, the ISSSTE or the Ministry of Health) and co-authors of some of the national clinical practice guidelines (diagnosis and management of hemophilia in pediatric and adult population). A guide for an interview intended to identify clinical practices and, hence, the consumption of institutional resources involved in the process of care, was created. In the analysis of the answer given by the experts, some parameters employed in the model were validated; the type and number of medical resources used in the follow-up of patients with hemophilia A or B were identified, the proportion of patients undergoing prophylaxis was identified, the type and quantity of medical resources associated with the care of bleeding episodes, by site of occurrence, were identified as well.

Epidemiology

The electronic document of the FHRM states that, by January 1, 2011, there were 4,725 individuals identified with any hemostatic factor deficiency[15]. This figure was applied the proportions of the different conditions (76.5% for hemophilia A, 11.5% hemophilia B and 12% others), reported by the World Federation of Hemophilia (WFH) 2011 global survey[16]. This way, the number of patients by type of hemophilia, as well as that of other coagulation disorders, was estimated. The prevalence of hemophilia A and B at the beginning of 2011 was estimated to be 3,616 and 541 patients, respectively, for a total of 4,157 cases. Based on the availability of data, the population was subdivided in children (< 19 years) and adults (≥ 19 years of age)[16].

The deceases correspond to the ICD D66X and D67X codes: Hereditary deficiency of factor VIII and factor IX, respectively, as reported by the National System of Information on Health (SINAIS – *Sistema Nacional de Información en Salud).* This source states that, in 2011, 39 deaths occurred that were attributed to hemophilia A and 3 to hemophilia B[17].

Incident cases are reported in an itemized way by hemostasis disorder type in the FMRM 2009-2011 statistical report. By December 31, 2011, there were 3,906 hemophilia A cases and 597 hemophilia B cases identified in the country[15]. These data were contrasted with the cases estimated at the beginning of that year, and this way, 346 hemophilia diagnoses were estimated to have been established in the year 2011: 290 of hemophilia A and 56 of hemophilia B (Fig. 1).

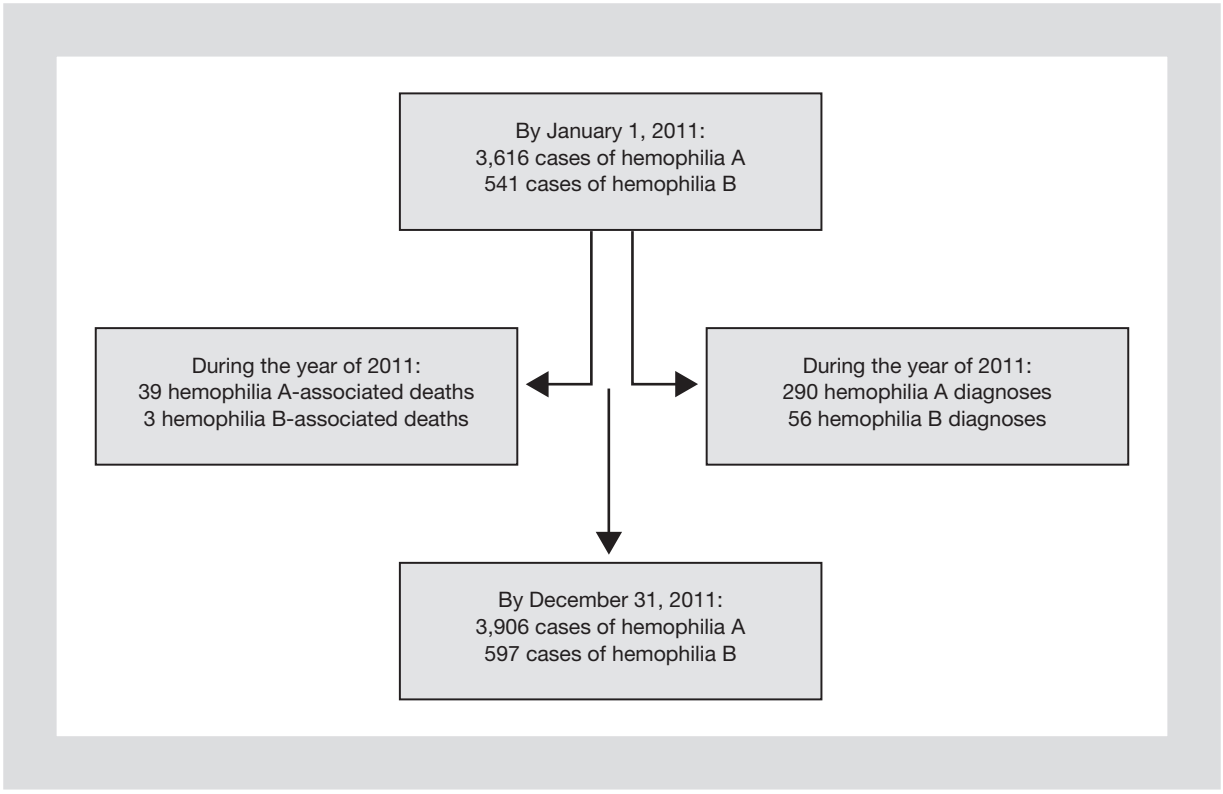

Figure 1. *Population of patients with hemophilia in Mexico in the year 2011.*

Direct costs estimation

Diagnosis

The cost of the diagnosis of the disease was established based on the laboratory tests that have to be performed in every patient suspected of having hemophilia, according to the indications described in the clinical practice guidelines Diagnosis and Treatment of Pediatric Hemophilia and Diagnosis and Treatment of Hemophilia in Adults[14]. The initial tests, such as blood count and clotting times, were estimated according to the unit costs at the IMSS current in 2011 for a secondary care hospital ($88 per test)[18]. Confirmatory tests (quantification of hemostatic factors and their corresponding inhibitors) and viral serology (human immunodeficiency virus [HIV], hepatitis B virus [HBV] and hepatitis C virus [HCV]) costs were estimated with the corresponding price at a tertiary care unit of the same institution and for the same year ($99 per test).

Monitoring or follow-up

The amount of each medical resource used in the routine follow-up of patients with a confirmed diagnosis of hemophilia was established by calculating the simple average of the answers provided by the expert panel. These resources were grouped into 4 categories: medical appointments (hematology and traumatology departments), laboratory tests, imaging studies and physical medicine and rehabilitation sessions. The employed unit costs correspond to those at an IMSS tertiary care unit in the year 2011[18]. For cost purposes, and considering that the time of the year when a patient is diagnosed with hemophilia is unknown, as well as the moment a patient dies because of this disease, these two subgroups were assumed to contribute on average with half of the observation period. Therefore, the incident cases and the deceases were imputed the cost corresponding to half year of follow-up.

Care of hemorrhagic events

Frequency and total number of hemorrhagic events

In order to estimate as accurately as possible the number of bleeding events occurred throughout the year, the proportion of patients on prophylaxis and the proportion of those who, as a complement, receive on-demand

treatment, were used as a basis. This calculation originated in the answers obtained from the expert panel, of which the values corresponding to the medians for the subpopulations of children and adults were taken. According to these answers, in 2011, only 30.0% of the children with hemophilia treated in public institutions of the National Health System received a prophylactic regimen and, therefore, the remaining 70.0% received on-demand treatment. In turn, in the adult population, only 8.0% received prophylaxis and 92.0% were on on-demand treatment.

Subsequently, the reports on bleeding episodes were considered by year for patients with hemophilia A. For the population on prophylaxis, the data of the work by Noone et al. was taken, which corresponds to 3 bleeding episodes/year in patients that have always been under this treatment regimen[19]. For the population that was receiving on-demand treatment, the hemorrhagic episodes average was considered according to the seriousness of the disease: for mild hemophilia A, the complement of an observation reported by Den Uijl et al.[20] was taken, which states that 61% of the patients with this condition did not suffer hemorrhages throughout a year and, therefore, 39% were assumed to have experienced at least one bleeding episode during the same period; thus, the value of 0.39 was regarded as the average of patients with mild hemophilia who sustain one hemorrhage/year. For patients with moderate hemophilia, the average number of hemorrhages was taken from a previous report[21], according to which, patients with moderate hemophilia A experience between 4 and 6 hemorrhages/year; and the intermediate value was taken: 5 hemorrhages/year. For the patients with severe disease, the expert opinion was resorted to, which indicated that there is at least one bleeding episode/week; therefore, the value was established on 52 hemorrhages/year. With these data, the weighted average was calculated considering the distribution of patients by seriousness, which is established in the FHRM 2009-2011 Report as of December 31, 2011[15]. This way, the yearly bleeding episodes average in the hemophilia A population that receives on-demand treatment was estimated to be 20.

Then, the expected number of hemorrhages was estimated for each population subgroup (children and adults, on prophylaxis and on on-demand treatment), from the proportion of children and adults on each one of this treatment modalities. These calculations were adjusted according to the patients' time at risk, i.e., a complete year was accounted for in the prevailing patients (alive at the end of the year), but for the deceases and the cases diagnosed during 2011, half of the bleeding events was considered on average. This way, 1,402 and 21,805 bleeding events were calculated during the year of study in children with and without prophylaxis, respectively. In turn, adults with and without prophylaxis were estimated to have suffered 524 and 40,186 bleeding episodes over the same period, respectively.

The calculation of bleeding events in patients with hemophilia B was made based on a work where the bleeding episodes in patients with hemophilia B versus hemophilia B are reported as having an 8.63/14.4 ratio[22]. This ratio was applied to the simple averages of hemorrhages in patients with hemophilia A by type of treatment and the subjects with hemophilia B who receive prophylaxis were estimated to experience 1.8 hemorrhages/year (3*[8.63/14.4]), whereas hemophilia B patients under on-demand treatment experience 12 hemorrhages/year ([20*[8.63/14.4]). The same procedure used for calculations in patients with hemophilia A was used for the patients with hemophilia B: the number of hemorrhages/year was calculated by subpopulations on prophylaxis and on on-demand treatment, according to the proportions of children and adults on each one of these treatment modalities and considering the patients' time at risk. The chldren without prophylaxis were estimated to have sustained 1,926 hemorrhages, whereas those who received prophylaxis suffered 124 events. In turn, adults with and without prophylaxis experienced 3,727 and 49 hemorrhages, respectively.

Average cost to manage a hemorrhage

The average cost for the management of the most common hemorrhages was calculated. The expenditure categories considered were listed on the section "Monitoring or follow-up". The consumption of each one of these resources for hemarthrosis, muscle hemorrhage (other than iliopsoas) and iliopsoas bleeding was determined based on the consulted experts' opinion and official unit costs of the IMSS in 2011[18]. In the case of cerebral hemorrhage, the cost corresponds to the updated value of the technical-medical cost derived for the IMSS diagnosis-related group (GRD – *Grupo Relacionado con el Diagnóstico)* 064 "Intracranial hemorrhage or cerebral infarction with complications and/or major comorbidities"[23]. For this purpose, the updating factor reported in the IMSS 2013 Unit Costs by Care Level listing was used[24]. The "other moderate hemorrhages" category was assigned the cost of a consultation at the emergency department[18], whereas in the case of other serious hemorrhages, the cost was

Table 1. Bleeding events distribution by anatomical site

Hemorrhage site	Children	Adults	Hospital discharge	Hospital stay
Hemarthrosis	75%	75%	0	0
Muscle	13.95%	14.80%	0	0
Iliopsoas	1.05%	0.20%	1	4.00
Central nervous system	0.35%	0.25%	1	9.32
Other (moderate)	8.65%	9.40%	0	0
Other (serious)	1.00%	0.35%	1	5.21
	100.0%	100.0%		

established as the sum of an emergency department consultation[18] plus an average of 5.21-day-hospital stay, a figure that corresponds to the hospitalization period indicated in the GRD 813 medical-economic official document "Coagulation disorders"[23].

Based on the answers of the expert panel, additional medications were not included as part of the resources required for the treatment of hemorrhages. Conversely, the cost of the basic resource for treatment, the hemostatic factor, was independently estimated in a particular category.

Total cost for the treatment of hemorrhagic events

The estimation of the total cost associated with the treatment of hemorrhages was based on the distributions by affected site reported in the national clinical practice guidelines[13,14]. The values corresponding to the medians of the reported data for hemarthrosis and muscle hemorrhage (other than the iliopsoas) in children and adults were used. In the cases of iliopsoas, central nervous system and "other site" hemorrhages (treated in the hospital setting), each event was assumed to correspond to a hospital discharge. To make sure for the costs of care not to be overestimated, the reports on hospital discharges and hospitalization days by modbidity of the SINAIS for the year of interest were used[17]. Table 1 shows the distribution of bleeding events by percentage. These percentages were applied to the number of hemorrhages estimated for each category (child or adult, with or without prophylaxis, hemophilia A or B). This way, the number of estimated events by anatomical site was obtained, which were multiplied by their respective average costs.

Consumption of hemostatic factors

The cost for the FVIII and FIX was estimated through the nation-wide consumption reports listed on the WFH Global Survey 2011[16]. By virtue of this report being itemized, it was possible to calculate the national expenditure for each factor (plasma-derived or recombinant FVIII and FIX). Since bypassing agents (rFVIIa) and anti-VIII factor inhibitor coagulant complex (FEIBA) employed in patients with high-responding inhibitors are not reported in the above mentioned source, the expenditure on these products was taken directly from data available at each institution. All acquisitions of the IMSS in the year of interest for the aforementioned products (in the case of rFVIIIa, for each one of its three presentations) were identified on this institution's procurement portal[25]. For the other public healthcare institutions, a search was conducted in the government procurement portal, and purchases by the ISSSTE and Petroleos Mexicanos healthcare services were identified[26] (that year, both these institutions were the only ones that purchased rFVIIa); this portal does not inform on other purchases of these products. According to the referred survey, the number of patients with high-responding inhibitors (95 and 5%, respectively) who received bypassing agents in 2011 was 192 with hemophilia A and 10 with hemophilia B[16].

Indirect costs estimation

Absenteeism (days/year missing work) of patients at working age and parents of children with hemophilia, differentiating single-parent families from those with both parents, was estimated. With data of the National Institute of Statistics and Geography (INEGI – *Instituto Nacional de Estadística y Geografía)*, the income/

worked hour and worked hours/week averages were obtained in the working population during the year 2011 in Mexico[27,28].

Based on the total number of hemorrhages in 2011 (see section "Care of hemorrhagic events"), the number of hemorrhages managed in the outpatient and hospital settings were calculated. Hospital stay total days were calculated considering the number of hemorrhages that required hospitalization and average hospital stay according to the bleeding site. The population was divided into younger and older than 14 years and this, in turn, was subdivided into 3 age subgroups (the subgroups were owing to data availability). Hospital stay-associated absenteeism was calculated for those younger and older than 14 years, as well as absenteeism associated with outpatient care. In the first case, one day of hospital stay equals to one day of absenteeism, whereas in the second case, each hemorrhage was regarded as causing the loss of half a working day (the patients attends the center to receive the factor and carries on with his activities). All cases were adjusted for participation in the job market. The proportion of < 14 year-old patients who live with one or both parents was estimated, as well as the probability of one or both them to be employed. Accordingly, the cases where the mother or the father loose one working day (or half) to bring the child to receive attention. Income loss due to absenteeism was calculated by multiplying the absenteeism days (due to hospital stay or outpatient care – half a working day –) for individuals younger and older than 14 years, by the "contribution to or participation in the workforce" (divided into younger and older than 14 years subjects) and by the average daily work-related income according to the INEGI.

Results

Cost per diagnosis

The cost per diagnosed case was estimated in $935. Since 346 cases (290 and 56 for hemophilia A and B, respectively) were diagnosed the year of interest, total cost for this category added up to $323,510 ($271,150 for hemophilia A and $52,360 for hemophilia B).

Cost per follow-up or monitoring

The yearly average cost for the follow-up or monitoring of one patient with hemophilia was estimated to be $11,346. The cost associated with the follow-up of patients with hemophilia A in 2011 was $17.67 million in subjects < 19 years and $24.78 million in those ≥ 19 years of age. For the patients with hemophilia B, these costs were $2.60 and $3.83 million pesos, respectively.

Cost for the care of hemorrhagic events

Average cost for the care of one hemorrhage

Table 2 shows the average cost estimates according to the affected anatomical site. The highest value corresponds to cerebral hemorrhages.

Total cost for the care of hemorrhagic events

Table 3 shows the average cost estimates for the care of bleeding episodes, itemized by category (children or adults, with or without prophylaxis, hemophilia A or B). Total expenditure for this category in the population with prophylaxis was $231 million, whereas in the population under on-demand treatment, the figure was $7.5 million.

Cost of hemostatic agents consumption

The itemized cost for the purchase of coagulation factors is shown in table 4. Patients with hemophilia A generated an expenditure of $579.6 million in this area. In patients with hemophilia B, the expenditure was $77.5 million.

Indirect costs

Daily work-related income during 2011 in Mexico was estimated to be $178.81. The daily work-related income product by the proportion of cases where there is absenteeism (calculated by age subgroups and according to the type of hemophilia and treatment), by the number of days of absenteeism, yields the estimated amount corresponding to indirect costs. A total of 24,697 effective days of absenteeism directly related to hemophilia were estimated during the year of interest. Consequently, the absenteeism-associated cost was $4.41 million.

Total costs

Table 5 shows the results for the costs of each one of the analyzed sources and shows the aggregated result for each type of hemophilia. Clearly, the expenditure on hemostatic factors is the main source of cost

Table 2. Average estimated cost for the care of one hemorrhage according to anatomical site

Hemorrhage site	Consultations*	Tests‡	Hospital stay	Total
Hemarthrosis	$ 3,193	$ 132	–	$ 3,325
Muscle†	$ 2,057	–	–	$ 2,057
Iliopsoas	$ 2,146	$ 800	$ 20,624	$ 23,570
Central nervous system§				$ 61,297
Other (moderate)	$ 1,803	–	–	$ 1,803
Other (serious)	$ 1,803	–	$ 26,863	$ 28,666

*Includes consultation with specialist (hematology and/or traumatology) and/or emergency department and/or physical medicine and rehabilitation sessions.
†Includes laboratory tests and/or imaging studies.
‡Other than the iliopsoas muscle.
§Corresponds to GRD 064 "intracranial hemorrhage or cerebral infarction with complications and/or major comorbidities", adjusted to the year 2011.

Table 3. Total cost for the care of hemorrhagic events

	Without prophylaxis		With prophylaxis	
Subpopulation	Events	Expenditure	Events	Expenditure
Hemophilia A				
Children	21,805	$ 80,360,962	1,402	$ 5,166,062
Adults	40,186	$ 131,345,489	524	$ 1,713,202
Hemophilia B				
Children	1,926	$ 7,096,563	124	$ 456,208
Adults	3,727	$ 12,182,251	49	$ 158,899
Total	67,644	$ 230,985,265	2,099	$ 7,494,371

Table 4. Cost for the consumption hemostatic factors

Factor	IU purchased	Cost per IU	Total cost
Hemophilia A			
FVIII (plasma-derived)	77,323,000	$ 4.42	$ 341,922,306
Recombinant FVIII	4,582,000	$ 8.65	$ 39,626,236
Recombinant FVIIIa			$ 168,832,067
aPCC			$ 29,244,840
Total expenditure on factors for hemophilia A			$ 579,625,449
Hemophilia B			
FIX (plasma-derived)	12,867,400	$ 5.23	$ 67,245,032
Recombinant FIX	N.R.	–	$ 0
Recombinant FVIIa			$ 8,793,337
aPCC			$ 1,523,169
Total expenditure on factors for hemophilia B			$ 77,561,538

since it represents 68.6 and 74.3% of total expenditure on hemophilia A and B, respectively. Noteworthy, the aggregate cost in hemophilia A is 8-fold higher than the cost in hemophilia B, with a patient volume 6.5-fold higher. However, when average costs per patient are compared, this ratio decreases drastically to 1.23.

Table 5. Total costs by source of cost and by type of hemophilia

	Hemophilia A	Hemophilia A
Cost per diagnosis	$ 271,150	$ 52,360
Cost per follow-up	$ 42,452,144	$ 6,439,020
Cost for the of care hemorrhagic events	$ 218,585,715	$ 19,893,920
Expenditure on hemostatic factors	$ 579,625,449	$ 77,561,538
Indirect costs	$ 4,044,607	$ 369,593
Total cost	$ 844,979,064	$ 104,316,431
Total patients with hemophilia in 2011	3,906	597
Average cost per patient in 2011	$ 216,328	$ 174,734

Sensitivity analysis

Table 6 displays the results of the performed deterministic sensitivity analyses, including each scenario's relative variation with regard to the estimations obtained in the base case. The variables that are most decisive on the results include the procurement cost of hemostatic factors (especifically the cost of bypassing agents) and the frequency of bleeding episodes and their medical treatment. The remaining parameters had a limited influence on the total economic impact estimation of hemophilia A and B in Mexico.

Discussion

In this study, the costs of hemophilia care were estimated within the context of public institutions of the National Health System in Mexico. For this purpose, all possible sources of costs throughout the process of care of these patients were included: diagnosis, regular follow-up and management of hemorrhagic events, with the population itemized according to the type of hemophilia, patient age (child or adult) and according with the type of treatment received, i.e., prophylactic or on-demand treatment. These data are complemented to a clinical level with the opinion of experts on hematology who practice at public health institutions (IMSS, ISSSTE and the Ministry of Health [SSA – *Secretaría de Salud*] and have wide experience. The study has a population-based approach, i.e., it analyses epidemiological data from national records on prevalent and incident patients, morbidity (hospital discharges) and mortality, all for a same time period. Therefore, the analysis is as thorough as possible for the most recent year for which all the necessary information was available at the moment the calculations were made (the year 2011).

The cost analysis showed that the investment on hemostatic factors is, by far, the main source of cost. In this area, recombinant factors are clearly not a significant source of cost yet (< 10% in hemophilia A and 0% in hemophilia B). Similarly, bypassing agents represent an important economic impact: in hemophilia A, this amounts to one third of the total cost of hemostatic factors, but these products are allocated to < 5% of patients. In the case of hemophilia B, the investment on bypassing agents is almost 13% of the entire expenditure on factors and they are used in < 2% of patients.

Although the second most important component of total cost is the management of hemorrhages, the investment on medical care due to bleeding events can be up to 76-fold higher in patients who receive on-demand treatment vs. those receiving prophylaxis ($131,345,489 vs. $1,713,202 in adults with hemophilia A). Although increasing the proportion of patients who receive prophylaxis entails a cost increase due to the purchase of hemostatic factors, data from this analysis show that prophylaxis drastically decreases the demand of healtcare services required to manage hemorrhages, not to mention the significant gain in terms of quality of life for the patients, as well as other potential direct or indirect savings resulting from patient overall improvement.

This study includes an analysis of indirect costs attributable to hemophilia as well; namely, the costs resulting from absenteeism caused by having to look for care in case of a hemorrhage. Although this is the component that contributes the least to total cost (< 1%), it is most likely to be underestimated: in the interviews

Table 6. Results of the univariate sensitivity analysis

Parameters and scenarios	Economic Impact Year 2011		Variation versus base case	
	Hemophilia A	Hemophilia B	Hemophilia A	Hemophilia B
BASE CASE	844,979,064	104,316,431	Reference	Reference
Hemophilia prevalence				
25% higher	876,225,307	107,433,182	–3.70%	–2.99%
Diagnosis cost				
20% lower	844,924,834	104,305,959	0.01%	0.01%
20% higher	845,033,294	104,326,903	–†0.01%	–0.01%
Follow-up cost				
20% lower	836,488,635	103,028,627	1.00%	1.23%
20% higher	853,469,493	151,604,235	–1.00%	–1.23%
Proportion on prophylaxis				
50% of the base case value	864,731,727	106,082,299	-2.34%	–1.69%
150% of the base case value	825,266,043	102,549,848	2.34%	1.69%
Hemorrhagic episodes*				
25% lower	789,321,126	99,250,508	6.59%	4.86%
25% higher	900,636,287	109,381,818	–6.59%	–4.86%
Hospitalized cases				
25% lower	837,886,850	103,676,609	0.84%	0.61%
25% higher	852,070,741	104,955,539	–0.84%	–0.61%
Cost of hemorrhages care†				
25% lower	790,332,635	99,342,951	6.47%	4.77%
25% higher	899,625,493	109,289,911	–6.47%	–4.77%
Expenditure on medications‡				
10% lower	787,016,519	96,560,277	6.86%	7.44%
10% higher	902,941,609	112,072,585	–6.86%	–7.44%
Cost per hour of absenteeism				
25% lower	843,967,912	104,224,033	0.12%	0.09%
25% higher	845,990,216	104,408,829	–0.12%	–0.09%

*Applies in patients with or without prophylaxis.
†Excludes the cost of hemostatic factors.
‡Includes hemostatic factors and bypassing agents.

with the clinical experts, it became clear that patients avoid as much as possible being admitted to receive in-patient care, mainly because the treatment is based on correcting the deficient coagulation factor levels and, given the chronic nature of the disease, often the patient attends the medical unit only looking for the factor. In this context, it is possible to think of scenarios where the patients are in no conditions to perform their work activities, but still refuse to be hospitalized.

The study does not only capture all potential sources of costs in the process of care of patients with hemophilia, but contrasts them to each other in order to minimize the risk of incurring relevant biases in the estimations. Concretely, both hospital discharges and days of hospital stay, as reported by the SINAIS[17] for patients with hemophilia in the year 2011, were employed as a reference at the moment the amount of hemorrhagic events occurred that year was estimated for the study population.

One of the main strengths of this study lies in the robustness of its data sources and its correspondence for the same time period. It should be highlighted that the proportion of patients receiving prophylactic treatment would seem to be gradually increasing in our country, so it is possible for this proportion to be currently higher than that contemplated in the present analysis.

This analysis shows that hemophilia A or B is an entity associated with considerable investments for public health institutions in Mexico (given the relatively

modest volume of patients), particularly in the care of serious hemophilia and of patients with high responding inhibitors. Although the main component of total investment is the acquisition of the hemostatic factor, the estimated expenditure for the care of hemorrhagic events is significantly higher in patients receiving on-demand treatment in comparison with those who receive prophylaxis. These results are not atypical: there is a large amount of previous information that has demonstrated the usefulness and lower cost of the use of prophylaxis in hemophilia patients in comparison with on-demand treatment[29-31]. Our data confirm these observations originating in other countries.

Conclusions

In Mexico, hemophilia is a health condition that requires large amounts of financial resources for its treatment, which are mainly allocated to the purchase of hemostatic factors and care of bleeding events, with the latter being lower in patients on prophylaxis with regard to patients undergoing on-demand treatment. Apparently, the cost of productivity loss does not significantly contribute to the total cost of the treatment of this condition.

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