

Research article

The estimated economic burden of genital herpes in the United States. An analysis using two costing approaches

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Abstract

Background: Only limited data exist on the costs of genital herpes (GH) in the USA. We estimated the economic burden of GH in the USA using two different costing approaches.

Methods: The first approach was a cross-sectional survey of a sample of primary and secondary care physicians, analyzing health care resource utilization. The second approach was based on the analysis of a large administrative claims data set. Both approaches were used to generate the number of patients with symptomatic GH seeking medical treatment, the average medical expenditures and estimated national costs. Costs were valued from a societal and a third party payer's perspective in 1996 US dollars.

Results: In the cross-sectional study, based on an estimated 3.1 million symptomatic episodes per year in the USA, the annual direct medical costs were estimated at a maximum of \$984 million. Of these costs, 49.7% were caused by drug expenditures, 47.7% by outpatient medical care and 2.6% by hospital costs. Indirect costs accounted for further \$214 million. The analysis of 1,565 GH cases from the claims database yielded a minimum national estimate of \$283 million direct medical costs.

Conclusions: GH appears to be an important public health problem from the health economic point of view. The observed difference in direct medical costs may be explained with the influence of compliance to treatment and possible undersampling of subpopulations in the claims data set. The present study demonstrates the validity of using different approaches in estimating the economic burden of a specific disease to the health care system.

Introduction

Herpes simplex virus type 2 (HSV-2) is the most frequent causative organism of genital herpes (GH) in the United States, while HSV type 1 is felt responsible for this recurrent infection in only 20 to 30 percent of cases [1]. GH is contagious both in the symptomatic and in the asymptomatic phase of the disease and causes painful

genital ulcers. The management of the patient involves consultations, laboratory exams and drug treatment for the disease and its complications.

GH is one of the three most widespread sexually transmitted diseases in the USA [2]. Published data show that 45 million persons aged 12 years or older have HSV-2 an-

tibodies [3], that up to 70% of patients attending sexual transmitted disease clinics have HSV-2 infection [4] and that the majority of patients with initially symptomatic GH will develop recurrent disease [5].

Cost of illness studies represent one of the applications of economic science to medicine. The aim of these studies is to assess the economic burden of a disease and to help decision-makers in targeting preventive efforts and allocating resources [6,7]. Despite its widespread and increasing transmission, there is still poor understanding of the economic impact of GH in the USA, which makes it difficult to evaluate societal costs and the cost-effectiveness of preventive efforts [8]. Therefore, the objective of the present study was to estimate the economic burden of GH in the USA, using two different costing approaches.

Methods

We conducted a population-based study on the costs of GH. In order to give a better estimate of the disease burden, we retrieved economic information using two different approaches: In the first instance, direct interviews were conducted with a random sample of office-based physicians using a structured, comprehensive questionnaire. Secondly, information was retrieved from a large, longitudinal administrative database. For this purpose, data from Diversified Pharmaceutical Services (DPS), which is a pharmaceutical benefit management firm, were used. For both approaches, the time span was one year (1996). Costs were referred to on a yearly basis and computed in 1996 US dollars. Data were collected and analyzed separately.

Approach using expert interviews

A questionnaire was administered to 30 randomly selected primary and secondary care physicians practicing in the North-East of the USA. Physicians were asked about the annual number of patients with GH and the total number of episodes of symptomatic GH, seeking medical care and treatment. Data collection included the following variables: (1) demographic characteristics of the physicians' practices; (2) epidemiological figures: number of patients with GH per year; stratification of patients according to age, gender, severity of disease recurrence rates; duration of episodes; and (3) resource utilization: frequency of consultations and laboratory tests for GH patients; prescription of drugs in first/recurrent episodes and duration of treatment; frequency of hospitalizations due to GH complications; employment of patients; proportion of patients unable to work.

The perspective of this analysis was societal; thus, both direct and indirect medical costs were based on the costs born by society. The US population in 1996 (279 million)

served as a reference. Regarding medical costs, the categories considered were the consultations and medical procedures performed, laboratory tests, pharmacological treatment and hospitalizations. Unit costs are illustrated in Table 1. For the purpose of this analysis, average monetary values from all respondents were considered [9]. Values used came directly from interviews with physicians involved in the study.

Indirect costs were calculated using the human capital approach [7, 10, 11]. These costs were based on an average U.S. hourly wage of \$14 [12], and were valued according to estimates of time consumed by hospitalization, time lost from work due to illness, and travel and waiting-room time resulting from physician visits. We estimated that individuals with a primary GH syndrome would miss two days of work if symptoms were not severe enough to require hospitalization, and one week of work if hospitalization was required. Patient travel and waiting room time was estimated to be two hours per physician visit. We did not use gender-specific wage rates, as females are underpaid relative to men [12], so that gender specific wage-rates would implicitly undervalue the costs of GH in females.

Approach using claims database

DPS is a pharmaceutical benefit service collecting and processing claims on consultations, laboratory tests, drug utilization and hospital treatment from Health Maintenance Organizations (HMOs) and Independent Practice Associations from different areas in the USA. For the present study, all patients diagnosed with GH who have been enrolled in the plans of four HMOs at any time during 1996 were included. The four health plans included in the analysis were located in the Southwest, East, Mid-West, and West of the USA. The approximately 0.5 million members enrolled in the health plans were generally employed or dependents of employed members. The majority of members reside in an urban rather than rural environment, representing an urban, working-class population. Less well represented in this population were the elderly (age over 65), the unemployed

Table 1: Unit costs per episode used in the physicians' study

Variable	Unit cost (\$)
Consultation	73.00
Clinical examination	40.33
Microbiologic evaluation	38.39
Complete blood count	21.29
Antibody testing	76.50
Urine analysis	12.59
Hospital day	669.00
Days off work	144.00

and those entitled to state medical assistance (6% of the plan members had Medicaid as their principal insurance).

Members were included if they had at least one claim for GH during the study period. We used the following International Classification of Disease-9 codes for data collection: 054.1 (GH); 054.10 (GH, unspecified); 054.11 (herpetic vulvovaginitis); 054.12 (herpetic ulceration of vulva); 054.13 (herpetic infection of penis) and 054.19 (other GH). For this analysis, the following definitions were used: "*prevalent case*" = members who had a GH diagnosis claim between the dates of 1/1/96 and 12/31/96; "*active case*" = members who had a GH diagnosis claim between the dates of 1/1/96 and 12/31/96, and had a drug claim for treating GH or were treated in the hospital for GH; "*incident case*" = members who had a GH diagnosis or drug claim in 1996 and no GH claim prior to 1996; "*recurrent case*" = members who were continuously enrolled in 1996, had a GH diagnosis or drug claim in 1996 and a recurrent claim 15 days or more after the first claim (incident cases excluded).

Direct medical costs were based on actual pharmacy, outpatient and hospital claims processed by DPS. Component costs were based on drug costs, outpatient costs, emergency room costs, inpatient costs, laboratory costs and home visit costs. Drugs used for treatment of GH were identified in members who also had a diagnosis claim for GH at some time during the study period. This allows for some reliance that the drug was used to treat GH and not some other form of herpetic infection. Mean, median, and standard deviation were calculated to describe the population statistics for costs. The perspective of this analysis was third party payer.

The annual costs attributable to GH-infection in the United States were estimated as the product of the number of incident and prevalent infections and the average present value of the costs attributable to a single GH-infection. We also evaluated the impact of other GH-associated complications such as neonatal herpes and excess cesarean sections. A crude estimate of the burden of these complications was calculated, based on data extracted from the DPS database and published data [1, 13,14,15,16].

Results

Approach using expert opinion

In the sample of 30 interviewed physicians, 15 were general practitioners (GPs), while 15 were specialists (6 dermatologists, 4 gynecologists, 3 infectious disease specialists and 2 urologists). Based on our data, GPs see on average 34 GH patients a year; among these patients 13 (38%) were reported to be primary cases. Specialists

see 56 GH patients per year, including 12 (21%) incident cases. Sixty-five percent of patients were in the 18-30 age group; 52% of patients were female. Almost half of the patients (49%) suffered from mild GH, whereas moderate and severe cases represented 37% and 14% of patients, respectively. Forty-eight percent of patients experienced less than 2 relapses a year, 36% 2 to 5 relapses and 16% more than 5 per year. A typical first GH episode was reported to last on average 10.8 days, slightly more than a typical recurrence (8.4 d). From the data available, the incidence of clinically manifest GH can be estimated to be 423,000 cases and the number of recurrent cases at about 698,000 patients in 1996. These estimates correspond to an occurrence rate of 3,139,000 symptomatic episodes.

Table 2 illustrates the total cost of illness obtained translating epidemiological figures and utilization rates in monetary terms using the unit cost values previously described. The estimated total burden of medical care for GH in the US in 1996 represents \$984 million, based on an estimated occurrence rate of 3.1 Mio symptomatic episodes. Of these costs, 49.7% were caused by drug expenditures, 47.7% by medical care and 2.6% by hospital costs. Further \$214 million represent the indirect costs to society. Thus, up to \$1.2 billion can be considered as being the total burden of GH to the US as computed with this methodology. Table 3 gives a breakdown of the costs at the single patient level.

Approach using claims database

Among 1,565 patients with GH, 65% of patients were in the 21-40 age group; 74% were female. Table 4 summarizes the main epidemiologic findings from this analysis. We extrapolated the collected data to the US population in 1996 (279 million) and calculated an annual incidence of 131,130 symptomatic GH cases in 1996, corresponding to a crude incidence of 0.47 per 1,000. The total number of persons with prevalent, active or recurrent symptomatic GH was estimated to be 806,310. This produces a crude prevalence of 2.89 cases per 1,000 in 1996.

Table 5 shows the costs of GH among DPS database enrollees. Costs were highest among recurrent cases and lowest among prevalent, symptomatic cases not requiring treatment. Using this approach, the amount of medical resources absorbed by the care of GH patients in the US can thus be estimated at \$244 million for 1996.

Based on previously published data [1, 13,14,15,16], we also estimated the direct costs of GH-associated complications. Neonatal herpes accounted for 400 annual cases with mean medical costs of \$60,000, whereas 6,000 excess cesarean sections contributed, on average, \$2,500 per case. Thus, the average cost of these GH-associated

complications can be estimated at \$39 million for 1996, bringing the total of the direct medical cost estimates to a sum of \$283 million.

Discussion

This report presents crude estimates rather than precise measures of the economic costs of GH in the USA. Using two different approaches, we estimated the total direct medical costs of GH to range from a minimum of \$283 million to a maximum of \$984 million in 1996. Indirect costs to society amounted to \$214 million due to production losses. Office-based medical care and drug treatment were the major sources of direct costs. Moreover, this study showed that the average GH patient seeking treatment is likely to be younger than 40, to develop

about 2 recurrent episodes, to undergo several laboratory exams, and to be treated with antiviral drugs. Relapses tended to be shorter than first episodes though having a higher cost per episode.

Our results are likely to be conservative estimates due to the great number of asymptomatic and shedding patients not seeking medical care and transmitting the disease to other individuals. As recently shown, the great majority of people with serologic evidence of HSV-2 infection have no history of recognized GH [3]. However, many seropositive persons shed HSV-2 that is detectable by culture from the genital tract, and many have symptoms that are directly referable to HSV-2 detectable by culture [17].

Table 2: Estimated costs of genital herpes in the USA (physicians' study)

	Costs (in thousands US\$)	% of direct costs	% of total costs
Consultations/lab testing (n)			
First episodes (422,950)	74,016		
1 to 2 (104,150)	19,684		
3 to 6 (468,650)	265,725		
7 or more (124,970)	110,224		
Subtotal	469,649	47.7%	
Drugs (n)			
First episodes (422,950)	27,069		
1 to 2 (104,150)	20,465		
3 to 6 (468,650)	303,685		
7 or more (124,970)	137,342		
Subtotal	488,561	49.7%	
Hospital (n)			
First episodes (422,950)	424		
1 to 2 (104,150)	1,250		
3 to 6 (468,650)	16,871		
7 or more (124,970)	6,998		
Subtotal	25,543	2.6%	
Total direct costs (n)			
First episodes (422,950)	101,508		
1 to 2 (104,150)	41,400		
3 to 6 (468,650)	586,281		
7 or more (124,970)	254,654		
Total	983,843	100%	82.1%
Total indirect costs (n)			
First episodes (422,950)	25,377		
1 to 2 (104,150)	9,373		
3 to 6 (468,650)	126,536		
7 or more (124,970)	52,487		
Total	213,773		17.9%
Total direct plus indirect costs			
First episodes (422,950)	126,885		
1 to 2 (104,150)	50,773		
3 to 6 (468,650)	712,817		
7 or more (124,970)	307,051		
Total	1,197,526		100%

Note: Costs are expressed in 1996 US\$.

Table 3: Average costs of genital herpes per patient in first and recurrent episodes

	First episode	%	% of total	Recurrent episode	%	% of total
Medical costs						
Consultations	62.6	35.8%		59.6	47.3%	
Clinical examination	39.8	22.7%		36.2	28.7%	
Microbiologic tests	17.6	10.1%		6.7	5.3%	
Antibody testing	12.8	7.3%		6.5	5.2%	
Complete blood count	4.6	2.6%		1.5	1.2%	
Urine analysis	4.6	2.6%		3.2	2.5%	
Others	33.0	18.9%		12.3	9.8%	
Total	175.0	100%	58.3%	126.0	100%	38.8%
Drug treatment						
Antiviral treatment	64.0	100%		131.0	100%	
Total	64.0	100%	21.3%	131.0	100%	40.3%
Hospital						
Hospitalization	1.0		0.4%	8.0		2.4%
Total direct costs	240.0		80.0%	265.0		81.5%
Indirect costs						
Production losses	60.0		20.0%	60.0		18.5%
Total costs per patient	300.0		100%	325.0		100%

Note: Costs are expressed in 1996 US\$.

Table 4: Epidemiology of genital herpes in the claims database

Age	Sex	Population	Prevalent GH		Incident GH		Recur- rent GH		Active GH	
			N	proportion/ 1,000	N	rate/1,000	N	rate/1,000	N	rate/1,000
0-20	Male	81,966	12	0.15	3	0.04	0	0	4	0.05
	Female	80,180	57	0.71	18	0.22	4	0.05	18	0.22
	Total	162,146	69	0.43	21	0.14	4	0.02	22	0.14
21-40	Male	70,026	141	2.01	32	0.46	21	0.30	58	0.83
	Female	84,067	455	5.41	105	1.25	42	0.50	162	1.93
	Total	154,093	596	3.87	137	0.89	63	0.41	220	1.43

Table 4: Epidemiology of genital herpes in the claims database (Continued)

41-60	Male	61,450	71	1.16	18	0.29	10	0.16	31	0.50
	Female	69,947	159	2.27	43	0.61	25	0.36	62	0.89
	Total	131,397	230	1.75	61	0.46	35	0.27	93	0.71
>60	Male	9,045	3	0.33	1	0.11	1	0.11	1	0.11
	Female	8,394	5	0.6	0	0	1	0.12	2	0.24
	Total	17,439	8	0.46	1	0.06	2	0.11	3	0.17
All	Male	222,487	227	1.02	53	0.24	32	0.14	94	0.42
	Female	242,588	676	2.79	167	0.69	72	0.30	244	1.01
	Total	465,075	903	1.94	220	0.47	104	0.22	338	0.73

Table 5: Direct medical costs of genital herpes among claims database enrollees and extrapolated US estimates

Type of patient	Mean cost (\$)	SD (\$)	Median cost (\$)	Mean total US costs (in Mio \$)
Incident GH	235	418	86	30.8
Prevalent GH	166	393	43	89.8
Active GH	355	536	191	21.8
Recurrent GH	499	707	359	101.6

Note: Costs are expressed in 1996 US\$.

From an economic point of view, it must be borne in mind that GH and other sexually transmitted infectious diseases have negative externalities in the sense that consequences of the disease are not only limited to people who have the disease but also to other people that can be potentially infected. This stems from the fact that consequences of risky sexual behavior are borne by the subject itself and by others via the transmission of the disease. In addition, it must be underlined that GH constitutes a risk factor for the spread of other sexually transmitted diseases (e.g. human immunodeficiency virus), which can be interpreted as a negative consequence of GH.

The estimates of the total direct medical costs obtained with the two different approaches are discrepant and can be explained, at least in part, with the influence of compliance to treatment. It must be noted that the higher figure is obtained with data collected via questionnaire and is likely to represent the monetary value of the amount of treatment prescribed by physicians. Moreover, the reported duration of primary and recurrent GH episodes in this analysis was longer than that commonly cited in the literature [5, 8, 17], which may have artificially increased the cost estimates. The lower figure, on the other hand, is an estimate based on claims and represents the mini-

um amount of medical care and treatment actually consumed by patients. This difference can be expressed as the difference from what is prescribed and what is actually consumed, i.e. compliance. Thus, the difference between the two global figures may be attributable to different utilization rates or different levels of compliance. A lower level of compliance means probably lower short-term direct costs, but probably higher indirect and long-term medical costs. The hypothesis of different utilization rates is also consistent with the psychological aspects of GH, which is perceived as a potential source of shame on patients [18] and is a plausible reason for lower levels of compliance to treatment.

In a recently published article by Tao *et al* [16], the national direct medical costs of GH were estimated at \$166 million annually for 1992-1994 (\$207 million in 1999 dollars), based on claims data from several sources. These numbers may be underestimates. Tao and colleagues [16] estimated that less than 30% of acyclovir claims not associated with a specific diagnostic code were provided for the treatment of GH. As drugs account for over half of the costs attributed to GH, underestimation of drug costs substantially decreases the estimated annual costs of GH.

Based on our estimates using the DPS claims database, GH seems to be a public health problem of important economic relevance. At least \$283 million can be estimated the direct health care costs attributable to GH, corresponding to 0.1% of the US health care expenditure (\$1,007,300 million). However, when computing for indirect costs and long-term complications (e.g. neonatal herpes, enhanced HIV transmission), the true costs may be greater than \$1.0 billion. In addition, this study has not been designed to give a monetary estimate of intangible costs of the disease. Psychological stress related to GH is well documented in the literature [18,19,20], and should be considered as a relevant factor of the total burden of illness, though not easily quantifiable.

As with any research study, limitations must be placed on the ability to generalize the results beyond the sample and setting employed. First, treatment for GH in the USA can be met at neighborhood health clinics, which offer confidential, low-cost treatment. Since a stigma is attached to the diagnosis of GH, patients may choose treatment at these clinics. The database had no information on these visits, since no claims were generated. Second, claims databases are collected for the purpose of payment to providers for the medical services rendered on behalf of enrolled members and rely on the coding of numerous medical events. Because of variations and incompleteness of coding, errors in identification and classification may occur. Coding is dependent on the diagnostic process, which is related to a clinician's training. Thus, the decision to diagnose GH by individual clinicians with different levels of expertise cannot be controlled within the boundaries of claims data. Third, the health plans included in this study allowed for geographical representation on a large regional basis. However, undetected patient, provider and practice differences may still exist. Caution should therefore be exercised in generalizing to other regions. Finally, cases selected may not necessarily be indicative of minority, low socioeconomic status, or indigent populations, since claims data can only provide data on those individuals who access the system. Therefore, the demographics of the database, in combination with the use of neighborhood clinics for GH treatment, make our calculated GH rates and costs lower bound estimates of the true GH prevalence and associated costs in the USA.

In conclusion, GH appears to be an important public health problem in the USA from the health economic point of view. The present study demonstrates the validity of using different approaches in analyzing the economic burden of a specific disease to the health care system.

Competing interests

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