

# Viral Meningitis-Associated Hospitalizations in the United States, 1988–1999

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## Key Words

Viral meningitis · Aseptic meningitis · Hospitalization costs · Hospitalizations

## Abstract

We used the National Hospital Discharge Survey and the Nationwide Inpatient Sample of the Health Care Cost and Utilization Project to estimate disease burden associated with viral meningitis hospitalizations in the United States. During 1988–1999, viral meningitis accounted for an estimated 434,000 hospitalizations (annual average, 36,000; average annual hospitalization rate, 14/100,000), and 2.1 million hospital days (annual average, 175,000). The estimated mean charge for viral meningitis-associated hospitalization during 1993–1997 varied between USD 6,562 and 8,313, resulting in annual estimated hospitalization costs between USD 234 and 310 million and a total estimated cost of nearly USD 1.3 billion for the 5-year period. In summary, viral meningitis remains an

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important cause of morbidity and financial burden and merits efforts to improve diagnostic, treatment, and prevention options.

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## Introduction

Although generally a benign and self-limited illness, viral meningitis often leads to hospitalization and diagnostic studies to rule out potentially life-threatening bacterial meningitis. In most cases, viral meningitis, commonly referred to as ‘aseptic meningitis’, is associated with enterovirus infection, although other viral agents, such as arboviruses, herpes simplex viruses, lymphocytic choriomeningitis virus, mumps virus, and others, can also be implicated [1, 2]. With the availability of new diagnostic tests for enterovirus meningitis [3–6] and ongoing development of new anti-enterovirus drugs [7], a better understanding of the burden of viral meningitis is important for developing and evaluating treatment, diagnostic, and prevention strategies.

Currently available estimates vary from 75,000 cases seeking medical attention to 2 million cases of aseptic meningitis occurring annually in the United States [1, 8, 9]. These estimates, however, are based on extrapolations from earlier etiologic studies in single institutions or from the nationwide aseptic meningitis surveillance, which was

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**Table 1.** ICD-9-CM codes for meningitis by etiologic category

| Etiologic category/diagnosis                                    | ICD-9-CM codes         |
|---|------------------------|
| <i>Viral meningitis</i>   |                        |
| Meningitis due to coxsackieviruses                              | 047.0                  |
| Meningitis due to echoviruses                                   | 047.1                  |
| Meningitis due to other specified enteroviruses                 | 047.8                  |
| Meningitis due to lymphocytic choriomeningitis virus            | 049.0                  |
| Meningitis due to adenovirus                                    | 049.1                  |
| Meningitis due to varicella-zoster virus                        | 053.0                  |
| Meningitis due to herpes simplex virus                          | 054.72                 |
| Meningitis due to mumps virus                                   | 072.1                  |
| Meningitis due to viruses not elsewhere classified              | 321.2                  |
| Viral meningitis not otherwise specified                        | 047.9                  |
| <i>Bacterial meningitis</i>                                     |                        |
| Meningitis due to salmonella                                    | 003.21                 |
| Tuberculous meningitis  | 013.0                  |
| Meningococcal meningitis  | 036.0                  |
| Gonococcal meningitis   | 098.82                 |
| Meningitis due to <i>H. influenzae</i>                          | 320.0                  |
| Pneumococcal meningitis   | 320.1                  |
| Streptococcal meningitis  | 320.2                  |
| Staphylococcal meningitis                                       | 320.3                  |
| Meningitis due to other specified bacteria                      | 320.8                  |
| Meningitis due to unspecified bacteria                          | 320.9                  |
| Meningitis in other bacterial diseases classified elsewhere     | 320.7                  |
| Meningitis due to congenital syphilis <sup>1</sup>              | 090.42                 |
| Meningitis due to secondary syphilis <sup>1</sup>               | 091.81                 |
| Meningitis due to syphilis not otherwise specified <sup>1</sup> | 094.2                  |
| Meningitis due to leptospirosis <sup>1</sup>                    | 100.81                 |
| <i>Fungal meningitis</i>  |                        |
| Cryptococcal meningitis   | 321.0                  |
| Meningitis in candidiasis                                       | 112.83                 |
| Meningitis in coccidioidomycosis                                | 114.2                  |
| Meningitis in histoplasmosis                                    | 115.01, 115.11, 115.91 |
| Meningitis in other fungal diseases                             | 321.1                  |
| <i>Unspecified meningitis</i>                                   |                        |
| Meningitis of unspecified cause                                 | 322                    |

<sup>1</sup> Meningitis due to spirochetes was combined with bacterial meningitis because of small numbers associated with each of these codes (between 0 and <0.1% of meningitis-associated discharges).

assumed to include only a small proportion of cases and was discontinued in 1994 [10].

In this study, we used the National Hospital Discharge Survey (NHDS) and the Nationwide Inpatient Sample (NIS) of the Health Care Cost and Utilization Project (HCUP) to estimate nationwide disease burden associated with viral meningitis hospitalizations in the United States. For comparison, we also analyzed hospitalizations associated with bacterial, fungal and unspecified causes of meningitis.

## Methods

Rates and epidemiologic patterns of meningitis-associated hospitalizations were determined by analyzing the NHDS data for the 12-year period from 1988 through 1999 obtained from the National Center for Health Statistics, Centers for Disease Control and Prevention (CDC) [11, 12]. Hospitalization costs were estimated, using the data from the NIS of the HCUP for 1993–1997, which contained information on inpatient stays from 900 to 1,000 hospitals in 17–22 states each year [13].

A meningitis-associated hospitalization was defined as one with at least one of the *International Classification of Diseases, Ninth*

Revision, Clinical Modification (ICD-9-CM) [14] codes for meningitis listed as a discharge diagnosis. Individual ICD-9-CM codes used in the study, grouped by etiologic category of meningitis, are listed in table 1.

Hospitalizations were analyzed by etiologic category of meningitis, year and month of discharge, patient's age, sex, duration of hospital stay, and standard census geographic region [15]. Due to the high proportion of missing race data (18.1%), no analysis by race/ethnicity was conducted [5, 16].

Hospitalization rates per 100,000 residents were calculated using denominators derived from US census [17] and natality [18] data. Of note, the results based on the NHDS are unreliable for hospitalization estimates <5,000 and are to be used with caution for estimates <9,000 [11]. The SUDAAN software was used to calculate standard errors (SEs) for hospitalization estimates to account for the NHDS stratified sampling techniques and to perform statistical comparisons by demographic characteristics, using two-sided t tests with weighted variance estimates [19, 20]. SEs and 95% confidence intervals (CIs) were calculated for hospitalization rates, using denominators obtained from vital records data that are considered free from sampling error [17, 18]. A weighted least-squares regression method was used as a test for trend in rates over time [21].

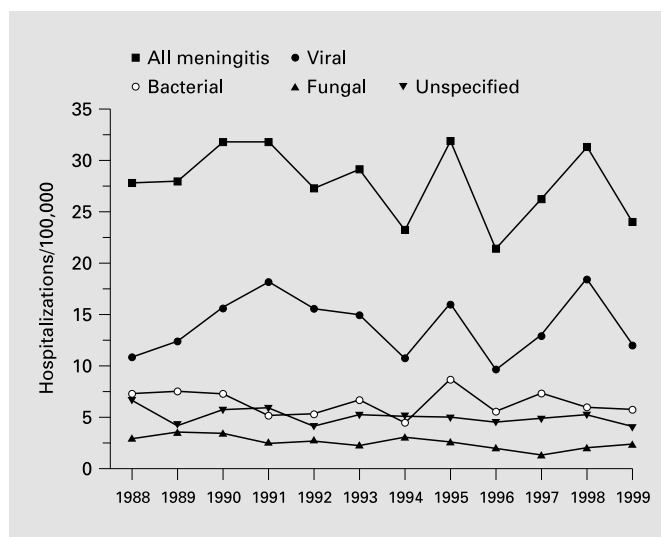
National charges for viral meningitis-associated hospitalizations were calculated from the HCUP NIS for 1993–1997 [13]. Annual mean and median estimates of charges were weighted using the weighting methodology of the HCUP [13], and the standard deviation and quartiles were calculated by the use of the SUDAAN software [19]. The annual estimated hospitalization cost associated with viral meningitis was calculated by multiplying the mean charge for a given year by the estimated number of hospitalizations for the year.

## Results

### Etiologic Categories

From 1988 through 1999, all causes of meningitis accounted for an estimated 865,058 hospitalizations (SE = 40,797) in the United States (table 2). There was an average of 72,088 meningitis-associated hospitalizations each year for an average annual hospitalization rate of 27.9/100,000 (95% CI, 25.3–30.4).

Viral meningitis, which accounted for 50.2% of all meningitis-associated hospitalizations (annual average, 36,183) was the most common etiologic category (table 2). Most cases of viral meningitis were listed as 'unspecified viral meningitis' (92% of viral meningitis-associated hospitalizations; annual average, 33,301), and few were attributed to enteroviruses (4.6%; annual average, 1,650) or other specific viral etiologies (3.5%; annual average, 1,242). The second most common etiologic category of meningitis was bacterial (23.1% of meningitis-associated hospitalizations; annual average, 16,686). Fungal meningitis accounted for 9.3% of meningitis-associated hospitalizations (annual average, 6,694), of which 71% were



**Fig. 1.** Meningitis-associated hospitalizations by etiologic category and year, NHDS, United States, 1988–1999.

**Table 2.** Meningitis-associated hospitalizations by etiologic category, NHDS, United States, 1988–1999

| Etiologic category | Hospitalizations (n = 865,058; SE = 40,797) |                                     |                  |
|--------------------|---|-------------------------------------|------------------|
|                    | n   | average annual hospitalization rate | percent of total |
| Viral              | 434,195 (24,205)                            | 14.0 (12.5–15.5)                    | 50.2             |
| Bacterial          | 200,234 (11,709)                            | 6.4 (5.7–7.2)                       | 23.1             |
| Fungal             | 80,325 (6,478)                              | 2.6 (2.2–3.0)                       | 9.3              |
| Unspecified        | 157,138 (10,360)                            | 5.1 (4.4–5.7)                       | 18.2             |

Rates are expressed per 100,000 population. More than one code for meningitis was listed for 0.8% of hospitalizations. Figures in parentheses indicate either SEs or 95% CIs.

coded as cryptococcal meningitis. Meningitis of unspecified etiology accounted for 18.2% of all meningitis-associated hospitalizations (annual average, 13,095). More than one etiologic category was coded in 0.8% of discharge records.

### Hospitalizations by Year, Sex, Age Group, and Geographic Region

The annual hospitalization rates for all causes of meningitis fluctuated widely over the study period, but no distinct overall temporal trend toward an increase or decrease in admissions was observed (fig. 1). However, the

**Table 3.** Meningitis-associated hospitalizations and hospitalization rates by etiologic category by sex, age group, and region, NHDS, United States, 1988–1999

|                               | Viral meningitis |                  | Bacterial meningitis |                 | Fungal meningitis |                | Unspecified meningitis |                | All meningitis |                  |
|-------------------------------|------------------|------------------|----------------------|-----------------|-------------------|----------------|------------------------|----------------|----------------|------------------|
|                               | rate             | n                | rate                 | n               | rate              | n              | rate                   | n              | rate           | n                |
| <i>Sex</i> <sup>1</sup>       |                  |                  |                      |                 |                   |                |                        |                |                |                  |
| Male                          | 14.5             | 220,121 (15,451) | 7.4                  | 112,854 (7,447) | 4.1               | 62,782 (5,471) | 5.7                    | 85,807 (6,961) | 31.5           | 477,152 (24,982) |
| Female                        | 13.5             | 214,074 (12,103) | 5.5                  | 87,380 (7,234)  | 1.1               | 1,754 (3,073)  | 4.5                    | 71,331 (5,913) | 24.4           | 387,906 (18,969) |
| <i>Age group</i> <sup>2</sup> |                  |                  |                      |                 |                   |                |                        |                |                |                  |
| <1                            | 213.3            | 102,086 (12,001) | 117.7                | 56,256 (5,916)  | 0.03              | 15 (14)        | 61.3                   | 29,315 (5,791) | 390            | 186,376 (19,930) |
| 1–4                           | 14.1             | 25,663 (3,462)   | 13.0                 | 23,599 (4,542)  | 0.03              | 60 (47)        | 6.8                    | 12,269 (2,050) | 33.7           | 61,313 (6,824)   |
| 5–19                          | 13.9             | 92,148 (9,631)   | 3.6                  | 24,170 (3,587)  | 0.02              | 1,544 (735)    | 2.0                    | 13,510 (2,572) | 19.5           | 129,651 (13,465) |
| 20–44                         | 14.0             | 168,976 (8,257)  | 2.9                  | 34,803 (3,513)  | 4.6               | 55,771 (5,347) | 3.3                    | 40,129 (4,035) | 24.6           | 297,240 (12,204) |
| 45–64                         | 4.8              | 29,479 (2,918)   | 4.5                  | 27,718 (2,451)  | 2.4               | 14,635 (2,442) | 4.5                    | 27,204 (3,317) | 16.1           | 98,289 (5,430)   |
| ≥65                           | 4.0              | 15,843 (2,716)   | 8.6                  | 33,688 (4,230)  | 2.1               | 8,300 (1,868)  | 8.8                    | 34,711 (4,133) | 23.5           | 92,189 (6,644)   |
| <i>Region</i> <sup>3</sup>    |                  |                  |                      |                 |                   |                |                        |                |                |                  |
| Northeast                     | 13.9             | 85,653 (7,684)   | 7.7                  | 47,260 (3,938)  | 3.1               | 18,802 (3,091) | 5.8                    | 35,780 (3,699) | 30.4           | 186,743 (13,646) |
| Midwest                       | 11.0             | 81,088 (11,723)  | 5.4                  | 39,461 (7,378)  | 1.7               | 12,797 (2,738) | 5.1                    | 37,187 (5,757) | 23.0           | 169,460 (24,593) |
| South                         | 14.2             | 153,691 (9,177)  | 6.2                  | 67,438 (6,665)  | 2.7               | 29,530 (3,904) | 5.2                    | 56,600 (5,707) | 28.1           | 303,724 (15,734) |
| West                          | 16.9             | 113,763 (17,399) | 6.8                  | 46,075 (4,758)  | 2.8               | 19,196 (3,111) | 4.1                    | 27,571 (5,291) | 30.4           | 205,131 (24,930) |

Rates are expressed per 100,000 persons of the corresponding population. Hospitalization estimates of  $\leq 5,000$  and corresponding rates are unreliable; estimates of  $\leq 9,000$  are to be used with caution [22].

<sup>1</sup> Significant p values for statistical comparisons by sex: bacterial,  $p < 0.01$ ; fungal,  $p < 0.001$ ; unspecified,  $p < 0.05$ ; all causes,  $p < 0.001$ .

<sup>2</sup> Significant p values for statistical comparisons across age groups: (1) <1-year-old group compared with each other age group,  $p < 0.001$ , except for fungal compared with 1- to 4- and 5- to 19-year-old

age groups; (2) 1- to 4-year-old group compared with 5- to 19-year-old group: bacterial, unspecified, and all causes,  $p < 0.001$ ; (3) 5- to 19-year-old group compared with 20- to 44-year-old group: fungal,  $p < 0.001$ ; unspecified, and all causes,  $p < 0.05$ ; (4) 20- to 44-year-old group compared with 45- to 64-year-old group: viral, bacterial, fungal, call causes,  $p < 0.001$ ; unspecified,  $p < 0.05$ ; (5) 45- to 64-year-old group compared with  $\geq 65$ -year-old group: bacterial, unspecified, and all causes,  $p < 0.001$ .

<sup>3</sup> Significant p value for statistical comparisons across regions: fungal, Northeast compared with Midwest,  $p < 0.05$ .

trends by etiologic category differed. For example, the annual estimates of viral meningitis-associated hospitalizations varied between 25,729 and 50,043 with peaks in 1990–1993, 1995 and 1998, and showed no significant temporal trend over the study period ( $p > 0.05$ ). The annual rates for bacterial meningitis-associated hospitalizations also fluctuated (fig. 1), but exhibited a small, but significant overall declining trend ( $p < 0.03$ ). This decline in bacterial meningitis-associated hospitalizations was only observed among children  $< 5$  years of age ( $p < 0.001$  for children  $< 1$  year and for children 1–4 years of age). Further analysis showed that overall rates declined significantly from 2.2/100,000 during 1988–1990 to 0.9/100,000 during 1997–1999 ( $p < 0.001$ ) for meningitis associated with *Haemophilus influenzae*, but not for meningococcal or other bacterial causes combined. Also, the proportion of *H. influenzae* meningitis among all bacterial meningitis-associated hospitalizations declined from 29.2% during 1988–1990 to 1.4% during 1997–1999. The rates of fungal meningitis-associated hospitalizations also

declined significantly over the study period ( $p < 0.01$ ). Although the overall hospitalization rates associated with unspecified meningitis remained unchanged ( $p > 0.05$ ), they did decline significantly among children aged  $< 1$  year ( $p < 0.05$ ).

Hospitalization rates for all causes of meningitis combined were significantly higher among males than among females ( $p < 0.001$ ; male/female ratio = 1.3; table 3). This difference between sexes was most prominent for fungal meningitis ( $p < 0.001$ ; male/female ratio = 3.6), apparently because of the association of cryptococcal meningitis with HIV infection. The male predominance in hospitalizations was observed to a lesser degree for bacterial ( $p < 0.01$ ) and unspecified ( $p < 0.05$ ) meningitides (male/female ratio = 1.3 for both), but not for viral meningitis.

The age at hospitalization for all causes of meningitis ranged widely between  $< 1$  and 99 years, with the median age being 20 years (mean age, 26.8 years). The median age at hospitalization was younger for viral and bacterial meningitides (13 and 10 years, respectively; mean age,

20.8 and 27.6 years, respectively) than for fungal (37 years; mean age, 40.6 years) and unspecified (29 years; mean age, 35.5 years) meningitides. For all causes of meningitis, children aged <1 year had by far the highest rate of hospitalization ( $p < 0.001$  for each of the age groups compared with children <1 year old; table 3). For viral meningitis, hospitalization rates decreased approximately 15-fold after 1 year through 44 years of age ( $p < 0.001$ ), and then declined approximately 3-fold more for persons  $\geq 45$  years old ( $p < 0.001$ ). For bacterial and unspecified meningitides, the rate of hospitalization decreased approximately 10-fold between <1 year and 1–4 years of age with smaller changes thereafter, and was followed by a 2- to 3-fold increase beginning with the 20- to 44- or 45- to 64-year-old age groups. Fungal meningitis-associated hospitalizations had a distinct pattern with very few cases in infants and children and most cases among young adults and the elderly, presumably representing an increased frequency of HIV infection and other conditions that predispose to immunosuppression in these age groups (table 3).

No remarkable differences in hospitalization rates across geographic regions were observed for all causes of meningitis or for individual etiologic categories (table 3).

#### Seasonal Patterns

The rates of meningitis-associated hospitalizations were highest in the summer months, but this seasonal pattern could be attributed to viral meningitis, for which 71.1% of hospitalizations occurred in the 6-month period from May to October. The other etiologic categories showed no clear seasonality (fig. 2).

#### Hospital Stay

Overall, during the 12-year study period, an estimated 8.2 million hospital days (SE = 459,968) were associated with all causes of meningitis, for an average of approximately 683,000 hospital days annually and an average hospital stay of 9.4 days (SE = 0.35; median, 4 days). Of these, approximately 2.1 million hospital days (SE = 172,987; 26%; annual average, 175,000) were associated with viral meningitis. Bacterial meningitis accounted for 3.0 million (SE = 200, 758; 36.6%; annual average, 250,000) hospital days, fungal meningitis accounted for 1.6 million (SE = 209,212; 19.5%; annual average, 133,000), and unspecified meningitis accounted for 1.5 million (SE = 137,285; 18.3%; annual average, 125,000) hospital days.

The duration of hospital stay varied by etiologic category and was shortest for viral meningitis (average, 4.7 days; SE = 0.31; median, 3 days) followed by unspecified

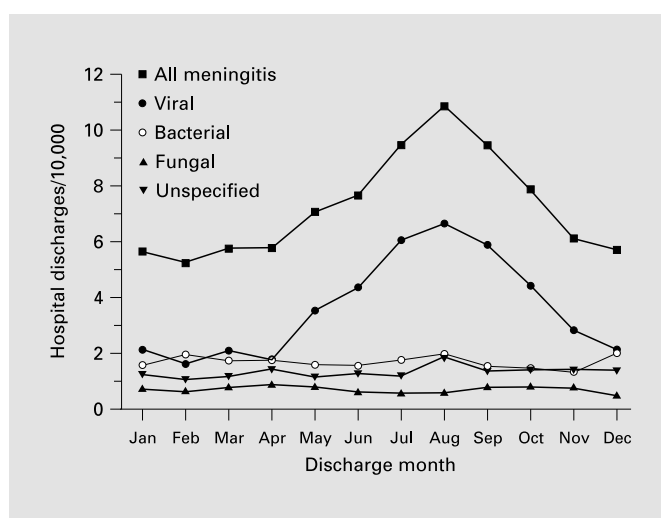


Fig. 2. Meningitis-associated hospitalization by etiologic category and month of discharge, NHDS, United States, 1988–1999.

meningitis (average, 9.3 days; SE = 0.64; median, 6 days). Bacterial (average, 15.3 days; SE = 0.7; median, 11 days), and especially, fungal meningitis-associated hospitalizations (average, 19.3 days; SE = 2.22; median, 11 days) had considerably longer duration.

#### Hospitalization Outcome

During the 12-year study period, an estimated 32,512 (SE = 3,061) or 3.8% of all meningitis-associated hospitalizations resulted in a patient's death. For viral meningitis, a fatal outcome was recorded for 0.4% of hospitalizations (1,678 deaths, SE = 781). The proportion of fatal outcomes was substantially higher for unspecified (4,834 deaths, SE = 892; 3.1%) and bacterial (16,708 deaths, SE = 2,243; 8.3%) meningitides and was the highest for fungal (9,704 deaths, SE = 1,448; 12.1%) meningitis, which is commonly associated with immunosuppression due to HIV infection or other causes.

#### Cost of Hospitalization

The estimated mean charge for viral meningitis-associated hospitalization during 1993–1997 varied between USD 6,562 and 8,313, resulting in estimated annual hospitalization costs between USD 234 million and 310 million (table 4) and a total estimated cost of nearly USD 1.3 billion for the 5-year period.

**Table 4.** Hospitalization costs associated with viral meningitis by year, United States, 1993–1997

| Year      | Charge <sup>1</sup> , USD |        | Hospitalizations <sup>2</sup><br>estimated number | Estimated hospitalization<br>cost, USD |
|-----------|---------------------------|--------|---|--|
|           | mean                      | median |   |  |
| 1993      | 6,562 (107)               | 4,462  | 38,573 (4,357)                                    | 253,116,026                            |
| 1994      | 8,300 (173)               | 5,040  | 28,140 (3,108)                                    | 233,562,000                            |
| 1995      | 7,359 (145)               | 4,662  | 42,095 (4,837)                                    | 309,777,105                            |
| 1996      | 8,313 (199)               | 5,081  | 25,729 (3,381)                                    | 213,885,177                            |
| 1997      | 8,260 (225)               | 5,065  | 34,467 (3,665)                                    | 284,697,420                            |
| 1993–1997 |                           |        |   | 1,295,037,728                          |

Figures in parentheses indicate SE.

<sup>1</sup> From the NIS of the HCUP.

<sup>2</sup> From the NHDS.

## Discussion

Meningitis leads to a substantial number of hospitalizations each year in the United States. Using the NHDS data, we estimated an average of 72,000 meningitis-associated hospitalizations per year between 1988 and 1999. The largest proportion of these, just over 50%, can be attributed to viral meningitis, with an estimated average of 36,000 hospitalizations and 175,000 hospital days each year.

As expected for a disease thought to primarily be associated with enterovirus infections [1, 2], the peak of viral meningitis-associated hospitalizations occurred in the summer and early fall, the disease was distributed equally among males and females, was most common in children, and manifested considerably greater year-to-year variability in the number and rate of hospitalizations than did the other attributed causes of meningitis. Not unexpectedly, the peak years for viral meningitis-associated hospitalizations occurred when surveillance data indicated widespread circulation of enterovirus serotypes commonly associated with community outbreaks of meningitis. For example, the 1990–1993 and 1998 peaks coincide with high activity of echovirus 30 in the United States. Echovirus 30, which has caused a number of aseptic meningitis outbreaks worldwide, was the most common enterovirus detected in the United States during 1990–1991, 1993, and 1998 and the second most common enterovirus during 1992 reported to the National Enterovirus Surveillance System at the CDC [22–24, CDC, unpubl. data]. The peak in 1995 coincides with high activity of echovirus 9, which accounted for 45% of reported enterovirus isolated that year [24]. The most common enteroviruses during the years with lower numbers of aseptic meningitis-associated hospitalizations were group B coxsackieviruses (type 5 in 1989 [22] and 1996 [23] and types 2 and 3 in 1994 [23]) and echovirus 11 in 1988 [25] and 1999 [24].

In this study, it was difficult to ascertain the contribution of individual etiologic agents of viral meningitis because most discharges (>90%) were coded as aseptic meningitis without stating the causative pathogen. This probably results from the limited clinical utility of conventional laboratory tests for detecting viral causes of meningitis [3, 6] and limited availability of viral diagnosis in routine practice. Furthermore, the specific ICD-9-CM codes for meningitis associated with some viral agents, such as arboviruses, do not exist. The possibility of miscoding and differences in coding practices across sampled hospitals is also a concern in interpreting the data on viral meningitis for the NHDS data set. However, the above-noted epidemiologic features of hospitalizations coded as viral meningitis suggest that, in the aggregate, these data provide a reasonable picture of viral meningitis hospitalizations in the United States.

This is the first estimate of the burden associated with viral meningitis in the United States, which is based on nationally representative data. The NHDS data set does, however, miss patients with viral meningitis who receive care in the emergency departments without admission or as outpatients. In previously published studies, the proportion of hospitalized viral meningitis cases ranged from 69–70% [26, 27] to 81% [28] and to 90% [29], with higher proportions noted during outbreaks of aseptic meningitis. Applying these proportions to our estimate of hospitalized cases, we could infer that, on average, between 40,000 and 52,000 patients seek health care for viral meningitis each year in the United States. This estimate is

lower than the previously reported 75,000 meningitis patients seeking medical attention [1]. Of note, it does not include cases who do not seek medical care (there are no data available to estimate this fraction) and therefore does not fully reflect the true incidence of viral meningitis. On the other hand, our estimate does not take into account repeated hospitalizations because the unit of analysis in the data sets used is not a patient, but a discharge. The data on the rates of repeated hospitalizations for viral meningitis are very limited. The only study which reported these data [9] indicated that only a relatively small proportion (11%) of patients are readmitted. Therefore, repeat hospitalizations should not have a substantial impact on our estimate of occurrence of viral meningitis.

The considerably shorter duration of hospital stay and a much lower proportion of hospitalizations with a fatal outcome in the group with viral meningitis is in agreement with viral meningitis being a less severe illness than that associated with other etiologic categories. Bacterial and fungal meningitides were associated with approximately 3-fold longer hospital stays and a substantially higher proportion of fatal outcomes (8.3 and 12.1%, respectively) than viral meningitis. Duration of the hospital stay and fatality for unspecified meningitis, which likely represents a mixture of viral, bacterial, and fungal etiologies, were in-between those for viral and the other two etiologic categories of meningitis.

The features of the hospitalizations associated with nonviral etiologic categories of meningitis that are also worth highlighting include a significant decrease in hospitalization rates during the study period in two groups – children aged <5 years with bacterial meningitis and patients with fungal meningitis. The decline in bacterial meningitis-associated hospitalizations among young children is likely associated with routine vaccination of infants with conjugate vaccines for *H. influenzae* type B (HiB), which was initiated in 1991 [30, 31]. Before the introduction of these vaccines, HiB was the leading cause of meningitis in young children [30]. The successful vaccination program resulted in a dramatic reduction in the occurrence of invasive HiB disease, including meningitis [31, 32]. The decline in the rates of fungal meningitis-associated hospitalizations is more difficult to evaluate because of relatively small numbers of hospitalizations in this category. However, it is likely related to advances in the management of fungal infections among immunocompromised patients, including those with HIV, achieved during the 1990s [33, 34].

Although the proportion of fatal cases is low and the median duration of hospitalization does not exceed 3

days, viral meningitis is associated with considerable financial burden. We estimated that between approximately USD 200 and 300 million were spent on viral meningitis-associated hospitalizations each year during 1993–1997, the period for which NIS data were available. Average charges per admission in our study are very close to the results of the only other published study based on the discharge data from multiple facilities, with reported mean hospital charges between USD 6,887 and 8,826 per admission [9]. The estimates of viral meningitis hospitalization costs reported in other studies are lower. The study utilizing decision analytic framework [8] and the analysis of hospital charges among infants  $\leq 18$  months of age at a single facility in 1995 [35] reported hospitalization costs between approximately USD 4,500 and 5,100 [8]. Two other papers, also based on the data from a single institution, reported even lower hospitalization costs. USD 1,757 [29] and 2,824 [36]. Additional research is needed to estimate the indirect costs (such as lost income due to missed work days, or costs of outpatient treatment for those who are not hospitalized) and to provide more complete estimate of costs associated with viral meningitis.

A considerable proportion of the hospitalization costs associated with viral meningitis is potentially preventable through rapid diagnosis. Rapid identification of the viral etiology would in many cases eliminate the need for further laboratory testing and unnecessary antibiotic treatment, and shorten or eliminate hospitalization [37]. Polymerase chain reaction assays for detecting enteroviruses have been shown to be rapid, highly sensitive, and specific in the diagnosis of enteroviral meningitis [3, 6]. Several studies have demonstrated the utility and cost effectiveness of these methods in patient management [4, 5, 37]. However, additional data are needed to demonstrate their impact on overall cost associated with enteroviral meningitis. Anti-enterovirus drugs currently under development could also be helpful in alleviating the disease burden associated with viral meningitis, as suggested by the preliminary data from clinical trials of pleconaril, a compound with broad antipicornavirus activity [7].

In summary, viral meningitis remains an important cause of morbidity and merits efforts to improve diagnostic, treatment, and prevention options.

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