



Published in final edited form as:

Pediatr Infect Dis J. 2014 November ; 33(11): 1119–1123. doi:10.1097/INF.0000000000000421.

Congenital Cytomegalovirus-related Hospitalizations in Infants <1 Year of Age, United States, 1997–2009

Adriana S. Lopez, MHS, Ismael R. Ortega-Sanchez, PhD, and Stephanie R. Bialek, MD

National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention (CDC), Atlanta, GA

Abstract

Background—An estimated 3600 infants born with congenital cytomegalovirus (cCMV) infection annually in the United States are symptomatic at birth. The proportion of infants with symptomatic cCMV infection who require hospitalization is unknown yet important for understanding the full disease and economic burdens of cCMV.

Methods—Data from the Healthcare Cost and Utilization Project Kids' Inpatient Databases were analyzed to determine numbers and rates of cCMV-related hospitalizations among infants for 1997, 2000, 2003, 2006 and 2009, the years the survey was conducted. A cCMV-related hospitalization was defined as a hospitalization with an International Classification of Diseases, 9th revision, Clinical Modification code of 771.1 in an infant without HIV or transplant-related codes. After applying hospital type-specific cost-to-charge ratios and adjusting to 2012 US dollars, total medical costs associated with cCMV-related hospitalizations were assessed. Results were extrapolated to represent national estimates.

Results—Among infants <1 year of age in the United States, an estimated annual average of 747 cCMV-related hospitalizations (18.6/100,000 per year) were coded during the 5 study years; 408 (55%) were among infants <1 month of age (122.0/100,000 per year). Approximately 4% of hospitalizations among infants <1 year resulted in death. Total estimated annual cost associated with cCMV-related hospitalizations among the US infants <1 year was at least \$14.3 million.

Conclusions—cCMV infection is associated with substantial numbers of hospitalizations, medical costs and mortality among the US infants. The true burden and costs of cCMV disease are likely much higher than our estimates when underascertainment of cCMV and total costs related to services and hospitalizations beyond the first year of life are considered.

Keywords

hospitalization rates; medical costs; congenital CMV

Approximately 28,000 infants are believed to be infected with congenital cytomegalovirus (cCMV) annually in the United States.^{1,2} An estimated 12.7% of these infants, about 3600

Address for correspondence: Adriana S. Lopez, MHS, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, 1600 Clifton Rd., NE, MS A-34, Atlanta, GA 30333. alopez@cdc.gov.

Supplemental digital content is available for this article. Direct URL citations appear in the printed text and are provided in the HTML and PDF versions of this article on the journal's website (www.pidj.com).

children annually, are symptomatic at birth, 40% or ~1400 of these children are estimated to develop permanent sequelae and 4% or ~140 to die as a result of infection.^{3–6} The spectrum of severity or the level of medical care that children with symptomatic cCMV infection require is not well described.⁷ We used data from a nationally representative sample of pediatric hospital discharges for the United States to estimate the numbers and rates of symptomatic cCMV-related hospitalizations among infants <1 year of age, describe the characteristics of infants hospitalized with symptomatic cCMV and estimate the medical costs associated with symptomatic cCMV-related hospitalizations.

Materials and Methods

Data Source

Hospital discharge records were extracted from the Kids' Inpatient Databases (KID) for 1997, 2000, 2003, 2006 and 2009. The KID are produced by the Healthcare Cost and Utilization Project (HCUP) within the Agency for Healthcare Research and Quality in collaboration with public and private statewide data organizations.⁸ The sampling frame for the KID includes a sample of pediatric discharges from all the US short-term, non-federal, general and other specialty hospitals recorded in state databases for 22, 27, 26, 38 and 44 participating states for 1997, 2000, 2003, 2006 and 2009, respectively. Systematic random sampling was conducted to select 10% of uncomplicated in-hospital births and 80% of complicated in-hospital births and other pediatric discharges for children 18 years in 1997 and 20 years in 2000, 2003, 2006 and 2009. The KID contain 2–3 million pediatric inpatient records from 2500 to 3500 hospitals per year.

Data Analysis

We defined a symptomatic cCMV-related hospitalization using the International Classification of Diseases, 9th revision, Clinical Modification (ICD-9-CM) codes as a hospitalization in an infant <1 year of age with a code for cCMV infection (771.1). We excluded those with codes for HIV (042) or transplant-related diagnoses [transplant (V42), transplant complication (996.8), transplant operation (E87.80)]. We examined symptomatic cCMV-related hospitalizations by sex, race/ethnicity, region of hospitalization based on standard census regions (Northeast, Midwest, South, West), hospital type (rural, urban teaching, urban nonteaching), hospital size (categorized by bed size as small, medium, large) and expected primary payer for hospitalization (Medicare, private insurance including health maintenance organizations, self-pay or other). We also examined symptomatic cCMV-related hospitalization by age group (<1, 1–3, 4–7 and 8–11 months) for those hospitalizations with age data available in months, over the 5 study years.

Symptomatic cCMV-related conditions were defined using International Classification of Diseases, 9th revision, codes as follows: microcephaly (742.1), hepatomegaly (789.1, 573.1), splenomegaly (789.2), thrombocytopenia (776.1, 287.3, 287.4, 287.5, 776.2), seizures (345, 779.0, 780.39), encephalitis (323, 058), other neurological symptoms (742), cerebral palsy (343), petechiae (772.6, 782.7), hearing loss (389, 315.34, 388.2) and chorioretinitis (363.0, 363.1, 363.2, 363.3). The presence of other conditions not specific to cCMV but that may occur in children with symptomatic cCMV, including low birth weight

[V213, 764, 765 (excludes 765.29)], jaundice [774 (excludes 774.0)], respiratory distress [769, 786, 770 (excludes 770.9), 799.1, 484.1, 518.81, 518.82, 518.83, 518.84, 519, 997.3], reflux (530.81, 530.11), hydrocephalus (331.4, 742.3) and failure to thrive (783.41), was also examined. Procedures potentially performed as the result of cCMV-related conditions were also examined, including mechanical ventilation (939.0, 939.1, 960.4, 967.0, 967.1, 967.2), feeding tubes (431.1, 431.2, 431.3, 431.4, 431.5, 431.6, 431.7, 431.8, 431.9, 449.9) and transfusions (990). In addition, procedures including cochlear implants, ventriculoperitoneal shunts, hip reductions and funduplications were examined but not presented because of small numbers.

The average annual number of days hospitalized was calculated by using the mean length of stay and multiplying by the average number of hospitalizations by year. Total medical costs for symptomatic cCMV-related hospitalizations were estimated among infants <1 year of age overall and by categories of age (<1, 1–3, 4–7 and 8–11 months), by converting total charges to costs using hospital-specific cost-to-charge ratios and adjusting for inflation to 2012 US dollars. Hospital-specific cost-to-charge ratios were not available for data from years 1997 and 2000; thus, the cost-to-charge ratios from 2009 differentiated by hospital size and type were applied to 1997 and 2000 to convert charges to medical costs. In addition, weights were adjusted according to HCUP methodology⁹ to account for hospitalizations with missing charges data. More conservative estimates of rates and costs of symptomatic cCMV-related hospitalizations were also calculated by excluding hospitalizations with a code only for respiratory distress (no other cCMV-related conditions present), since respiratory distress alone is not a typical presentation of symptomatic cCMV.

Because individual identifiers are not available in the KID, the hospital discharge record was used as the unit of analysis and the numbers of discharges, rather than numbers of infants, with symptomatic cCMV-related hospitalizations were analyzed. The symptomatic cCMV-related hospitalization numbers, rates and associated costs that we present are extrapolations from hospitalizations without missing age information to represent national estimates. Specifically, national estimates for the number of symptomatic cCMV-related hospitalizations, length of stay and total medical costs associated with hospitalization were calculated using the discharge weights developed for the HCUP.⁸ Estimates with a relative standard error >0.30 are considered statistically unreliable and are thus not presented.¹⁰

Rates of symptomatic cCMV-related hospitalizations were calculated as the estimated number of hospitalizations per 100,000 infants <1 year and <1 month of age using data from the US Census as the denominator. The denominator for infants <1 month of age was calculated by dividing the population for infants <1 year of age by 12, while the numerator included only estimated numbers for hospitalizations among infants with known age in months. Denominators obtained from vital records data were considered free from sampling error. Standard errors (SEs) and 95% confidence intervals (CIs) were calculated using SUDAAN release 10.0.1 (SAS Institute Inc., Cary, NC) to account for the complex survey design of the KID. Poisson regression was used to estimate statistical differences in incidence over the 5 study years and among major US geographical regions.

Results

Symptomatic cCMV-related Hospitalization Rates and Characteristics

During the 5 study years, an estimated total of 3734 symptomatic cCMV-related hospitalizations occurred among infants <1 year of age in the United States. Of the total hospitalizations, 2755 (73.8%) had age data available in months; the median age of symptomatic cCMV-related hospitalizations was 0 months (mean: 1 month, range: 0–11 months).

The estimated average number of annual symptomatic cCMV-related hospitalizations for all infants <1 year of age in the United States was 747 (range 677–823) with an overall annual estimated rate of 18.6 (95% CI: 18.5–18.7) per 100,000. Trends in symptomatic cCMV-related hospitalization rates did not differ significantly over the study period or across the US regions (Table 1). Non-Hispanic whites represented the greatest proportion of symptomatic cCMV-related hospitalizations (35.1%) but non-Hispanic blacks had the highest rate (23.5/100,000; $P = 0.001$) (Table 1). The majority of symptomatic cCMV-related hospitalizations occurred in hospitals classified as large (60.6%) and as urban teaching (72.3%) (Table 1). More than half of hospitalizations were covered by Medicaid (59.0%) and private insurance or health maintenance organizations were responsible for payment of 32.5% of hospitalizations.

Of symptomatic cCMV-related hospitalizations in the United States among infants <1 year, 2042 (74.1%) were among infants <1 month, 403 (14.6%) among infants 1–3 months, 167 (6.1%) among infants 4–7 months and 143 (5.2%) among infants 8–11 months of age (Table 2). The estimated average number of annual symptomatic cCMV-related hospitalizations for infants <1 month of age was 408 (range 350–459) with an overall annual estimated rate of 122.0 (95% CI: 121.9–122.1) per 100,000. Among the symptomatic cCMV-related hospitalizations in infants <1 month of age, up to 60% had a code for at least 1 cCMV-related condition, with thrombocytopenia (48.3%) occurring most frequently. Low birth weight and respiratory distress were also common (58.0% and 52.6%, respectively); 36.4% of hospitalizations had codes for mechanical ventilation and 23.1% for transfusions (Table 2). The most commonly coded cCMV-related conditions among older infant hospitalizations were thrombocytopenia (19.6%) among infants 1–3 months of age and seizures among infants 8–11 months of age (30.8%). Respiratory distress was common among symptomatic cCMV-related hospitalizations in infants 1–7 months of age; the proportion of symptomatic cCMV-related hospitalizations with a code for pneumonia increased from 5.4% in <1-month olds to 15.7% in 8–11-month olds. The proportion of symptomatic cCMV-related hospitalizations with codes related to mechanical ventilation decreased from 36.4% among infants <1 month of age to 17.4% in infants 1–3 months of age.

An estimated 157 (4.2%) symptomatic cCMV-related hospitalizations among infants <1 year ended in death; 88 (90.7%) were among infants <1 month of age. Among the estimated 157 deaths among infants <1 year, 63.0% were male and 36.8% were non-Hispanic white; 42% occurred in infants with birth weight <1500 g. Thrombocytopenia was the most common cCMV-related code among the hospitalizations that ended in death (59.0%); respiratory distress was coded for in 85.2% and 30.2% had a neurologic code (ie, seizures,

microcephaly, other neurological symptoms). Of the 111 (69.8%) deaths that did not have a neurologic code, 84.9% had a code for respiratory distress, 67.9% for low birth weight and 68.5% for thrombocytopenia.

Length of Stay and Cost of Symptomatic cCMV-related Hospitalizations

Overall, an estimated total number of 108,299 days (26,660 days annually) were associated with symptomatic cCMV-related hospitalizations during the 5 study years among infants <1 year of age; 86.8% of the days hospitalized were accounted for by hospitalizations among infants <1 month of age, of which 54.4% were among infants <1 month who were <1500 g. The median length of hospitalization was 12.9 days (quartile range: 5–37 days) among infants <1 year, 15.5 days (quartile range: 6–45 days) among infants <1 month and 4.9 days (quartile range: 2–12 days) among infants 1–11 months of age. The median costs for hospitalization among infants <1 year, <1 month and 1–11 months of age were \$19,100, \$25,500 and \$7600, respectively (Table, Supplemental Digital Content 1, <http://links.lww.com/INF/B927>). Among infants <1 month, median length of hospitalization and cost were higher among those <1500 g compared with infants ≥1500 g (67.4 days and \$102,300 versus 11.1 days and \$17,600). Of the total annual costs of \$14.3 million for symptomatic cCMV-related hospitalizations among infants <1 year of age, \$10.4 million (72.7%) was accounted for by hospitalizations among infants <1 month of age, of which \$10.1 million (97.6%) was accounted for by hospitalizations in infants <1 month with birth weight <1500 g. The total annual cost for symptomatic cCMV-related hospitalizations that ended in death was \$1.7 million.

Excluding hospitalizations with codes only for respiratory distress resulted in more conservative estimates of symptomatic cCMV-related hospitalizations and costs of 3030 total hospitalizations among children <1 year of age or 606 hospitalizations annually (15.1/100,000) for an estimated annual cost of \$10 million.

Discussion

Using nationally representative hospital discharge data, we estimate that at least 747 symptomatic cCMV-related hospitalizations resulting in ~21,700 hospitalization days occur each year among infants <1 year, with just over half (55%) of the hospitalizations occurring among infants <1 month of age. An estimated 4% of the symptomatic cCMV-related hospitalizations ended in death. Costs were the highest for hospitalizations among infants <1 month and those with birth weight <1500 g, which accounted for the bulk of the symptomatic cCMV hospitalization costs in the first year of life. Considering hospitalizations in the first year of life alone, symptomatic cCMV is associated with sizable morbidity, mortality and substantial medical costs, estimated to range from at least \$10 to \$14.3 million annually. The true costs of symptomatic cCMV disease among infants and young children are likely much higher than our estimates when costs related to services associated with feeding tubes, mechanical ventilation, specialized equipment, cochlear implants, re-evaluations, special education, hearing aids and hospitalizations beyond the first year of life are considered.⁷

Data from a systematic review of population-based studies estimated that 12.7% of cCMV-infected infants are symptomatic at birth,³ which would translate to approximately 3600 symptomatic infants born annually in the United States. The proportion of these infants with disease severe enough to require hospitalization is not known. Dividing the average annual estimated number of symptomatic cCMV-related hospitalizations identified in our study for infants <1 month (408) by the estimated expected number of children born with symptomatic cCMV (3600) suggests that only ~11% of the expected total number of infants with symptomatic cCMV infections had a cCMV-coded hospitalization. While symptomatic cCMV disease may not be severe enough to warrant hospitalization in all cases, it is likely that some proportion of infants with symptomatic cCMV infection goes undiagnosed or is not coded for and thus their conditions are not attributable to cCMV.

About 40% of the hospitalizations among infants <1 year with a cCMV code did not have codes for any cCMV-related conditions, raising the question of whether these hospitalizations were related to symptomatic cCMV infection. Signs and symptoms classically associated with cCMV, even when present, may not be comprehensively coded for in administrative data. As such, it is likely that we underascertained the number of cCMV-related conditions among those with a symptomatic cCMV-related hospitalization. It is possible that some of the hospitalizations we defined as cCMV-related may have occurred in infants whose hospitalizations were due to other conditions in whom asymptomatic cCMV infection was detected. However, it seems unlikely that there would have been many hospitalizations in which cCMV infections that did not contribute to the need for hospitalization would have been coded for in discharge data. We identified codes for respiratory distress in about 50% of the symptomatic cCMV-related hospitalizations among infants <1 year and <1 month. Although respiratory distress alone is not typically recognized as symptomatic cCMV, respiratory distress and lung disease have been described previously in infants with congenital infection.¹¹ The extent to which respiratory distress was directly the result of cCMV infection or a result of prematurity, to which cCMV infection may have contributed, is unclear.

Information on symptomatic cCMV-related hospitalizations in the United States is limited and comes from data collected before 1990.¹² Consistent with a study of symptomatic newborns with cCMV conducted in Alabama,¹² we found that the median duration of hospitalization was longer among low birth weight compared with full-term infants. Compared with admission rates for cCMV-related hospitalizations among infants <1 month of age in Australia (443/100,000),¹³ the overall rate for symptomatic cCMV-related hospitalizations in infants <1 month of age in our study was almost 4 times lower (122/100,000). At least 2 reasons may explain such differences: (1) we excluded hospitalizations with HIV or transplant-related codes and (2) ascertainment of symptomatic cCMV infection may have been more complete in the Australian study. Without medical record validation and laboratory testing, we do not know the extent to which all infants with symptomatic cCMV are diagnosed. To better understand the true hospitalization burden in infancy that results from symptomatic cCMV infection, the proportion of infants with cCMV disease that is severe enough to require hospitalization and the extent to which cCMV disease is currently ascertained require additional study.

Published estimates of cCMV-related mortality among symptomatic children range from 4% to 30%.^{2,12,14,15} The annual number of deaths among infants <1 month and <1 year of age in the United States due to cCMV were estimated in our study to be 18 and 31, respectively. Extrapolating data from a population-based study of cCMV mortality in the United States by taking the total number of deaths for each age group in that study and dividing by the 17-year study period¹⁶ yields similar numbers of deaths, 19 and 33 among infants <1 month and <1 year of age, respectively. In our study, the majority (70%) of hospitalizations among infants <1 year of age ending in death had codes for respiratory distress, low birth weight and/or thrombocytopenia. In contrast to a longitudinal study of children with symptomatic cCMV infection during infancy in which all infants who died had severe neurologic damage,¹⁴ only slightly less than a third of the deaths in our study were associated with a code for a neurologic condition (30%). The explanation for these differences is unclear as it seems likely that severe neurologic conditions, had they been present, would have been captured in hospitalization data. Hospitalization data may provide relatively complete estimates of the number of recognized cCMV-related deaths, as most deaths likely occur in hospitals, but they are likely not complete in listing all of the cCMV-related complications that may have led to the death. Additional studies are needed to better understand the extent to which additional cCMV-related deaths are occurring among hospitalized infants but go undiagnosed.

Our study was subject to limitations. By using hospital discharge data we were limited to estimating numbers of symptomatic cCMV-related hospitalizations in which cCMV infection was diagnosed and coded. The extent to which this overestimates the number of infants with symptomatic cCMV who require hospitalization depends on how commonly infants with cCMV require multiple hospitalizations in the first year of life. Our estimates of symptomatic cCMV-related hospitalizations among infants <1 month of age are underestimates as data on age in months was suppressed by some states and our extrapolations were based only on those hospitalizations with available data on age in months. Furthermore, our data did not allow us to determine if cCMV was the principal cause of hospitalization. Our inclusion of all hospitalizations with a code for cCMV may have overestimated symptomatic cCMV hospitalization rates by including some hospitalizations in which cCMV infection was present but did not contribute to the hospitalization. However, given that cCMV infection is not routinely screened for in the United States, this seems unlikely. Coding practices for cCMV-related hospitalizations have not been assessed and we may have missed symptomatic cCMV-related hospitalizations that were coded for using the CMV code (078.5), which does not specify congenital infection. Including the CMV code (078.5) in our case definition for symptomatic cCMV-related hospitalizations would have captured an additional 1576 hospitalizations among infants <1 year, increasing the hospitalization rate by 30%, but would only have increased the hospitalization rate among infants <1 month by 14%. Data on treatments given during hospitalization were not available in the discharge records nor were laboratory testing results, which may have provided confirmation of a cCMV diagnosis. It is likely that a portion of the stay and costs among infants born <1500 g were not related to cCMV and we overestimated costs for this group; however, cCMV has been shown to cause low birth weight.^{14,17,18}

Our analysis illustrates the substantial disease and economic burden of symptomatic cCMV among infants <1 year of age in the United States with costs of hospitalizations estimated to range from at least \$10 to \$14.3 million annually. However, hospitalizations reflect only a part of the costs associated with symptomatic cCMV during the first year of life. cCMV has been identified as the leading infectious cause of neurodevelopmental disabilities and impairments, affecting similar numbers of children as Down syndrome.¹⁹ Further research is needed to better understand the full impact of the burden of disease of symptomatic cCMV during the first year of life and throughout the life span. Although hospital discharge data likely underestimates the true number of symptomatic cCMV-related hospitalizations, these data can be useful for tracking trends and providing estimates of the burden of severe, symptomatic cCMV infection and, in the future, monitoring impact of prevention strategies.

Acknowledgments

This research was completed while the primary authors were employees of the Centers for Disease Control and Prevention (CDC). No funding was secured for this study. None of the authors have financial relationships relevant to this article to disclose. None of the authors have conflicts of interest to disclose. The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

References

1. Demmler GJ. Infectious Diseases Society of America and Centers for Disease Control. Summary of a workshop on surveillance for congenital cytomegalovirus disease. *Rev Infect Dis.* 1991; 13:315–329. [PubMed: 1645882]
2. Ross SA, Boppana SB. Congenital cytomegalovirus infection: outcome and diagnosis. *Semin Pediatr Infect Dis.* 2005; 16:44–49. [PubMed: 15685149]
3. Dollard SC, Grosse SD, Ross DS. New estimates of the prevalence of neurological and sensory sequelae and mortality associated with congenital cytomegalovirus infection. *Rev Med Virol.* 2007; 17:355–363. [PubMed: 17542052]
4. Cannon MJ. Congenital cytomegalovirus (CMV) epidemiology and awareness. *J Clin Virol.* 2009; 46(4):S6–S10. [PubMed: 19800841]
5. Kenneson A, Cannon MJ. Review and meta-analysis of the epidemiology of congenital cytomegalovirus (CMV) infection. *Rev Med Virol.* 2007; 17:253–276. [PubMed: 17579921]
6. Ludwig A, Hengel H. Epidemiological impact and disease burden of congenital cytomegalovirus infection in Europe. *Euro Surveill.* 2009; 14:26–32. [PubMed: 19317969]
7. Grosse, SD., Ortega-Sanchez, IR., Bialek, SR., Dollard, SC. The economic impact of congenital CMV infection: methods and estimates. In: Reddehase, MJ., editor. *Cytomegaloviruses: From Molecular Pathogenesis to Intervention.* Norfolk: Caister Academic Press; 2013. p. 49-55.
8. Healthcare Cost and Utilization Project. Introduction to the HCUP Kids' Inpatient Database (KID) 2009. Rockville, MD: Agency for Healthcare Research and Quality; 2011.
9. Healthcare Cost and Utilization Project. Kids' Inpatient Database (KID) User Guide. Rockville, MD: Agency for Healthcare Research and Quality; 2011. Cost-to-Charge Ratio Files: 2009.
10. Klein RJ, Proctor SE, Boudreaux MA, et al. Healthy People 2010 criteria for data suppression. Healthy People 2010 statistical notes: from the Centers for Disease Control and Prevention/ National Center for Health Statistics. 2002:1–12.
11. Coclite E, Di Natale C, Nigro G. Congenital and perinatal cytomegalovirus lung infection. *J Matern Fetal Neonatal Med.* 2013; 26:1671–1675. [PubMed: 23570320]
12. Boppana SB, Pass RF, Britt WJ, et al. Symptomatic congenital cytomegalovirus infection: neonatal morbidity and mortality. *Pediatr Infect Dis J.* 1992; 11:93–99. [PubMed: 1311066]

13. Seale H, Booy R, MacIntyre CR. Trends in hospitalizations for diagnosed congenital cytomegalovirus in infants and children in Australia. *BMC Pediatr.* 2009; 9:7. [PubMed: 19171068]
14. Pass RF, Stagno S, Myers GJ, et al. Outcome of symptomatic congenital cytomegalovirus infection: results of long-term longitudinal follow-up. *Pediatrics.* 1980; 66:758–762. [PubMed: 6159568]
15. Townsend CL, Peckham CS, Tookey PA. Surveillance of congenital cytomegalovirus in the UK and Ireland. *Arch Dis Child Fetal Neonatal Ed.* 2011; 96:F398–F403. [PubMed: 21289013]
16. Bristow BN, O'Keefe KA, Shafir SC, et al. Congenital cytomegalovirus mortality in the United States, 1990–2006. *PLoS Negl Trop Dis.* 2011; 5:e1140. [PubMed: 21541359]
17. Weller TH, Hanshaw JB. Virologic and clinical observations on cytomegalic inclusion disease. *N Engl J Med.* 1962; 266:1233–1244. [PubMed: 14040222]
18. Berenberg W, Nankervis G. Long-term follow-up of cytomegalic inclusion disease of infancy. *Pediatrics.* 1970; 46:403–410. [PubMed: 4318343]
19. Lanzieri, TM., Lopez, AS., Grosse, SD., Bialek, SR. Updated estimates of the burden of congenital cytomegalovirus as a cause of developmental disabilities or impairments: a comparative perspective. CMV 2012 4th Congenital CMV Conference & 14th International CMV/ Betaherpesvirus Workshop; San Francisco, California. October 29 to November 2, 2012; Milan, Italy: M.C.A. Events; 2012. Abstract A24

Table 1
Estimated Numbers and Rates of cCMV-related Hospitalizations Not Associated With
HIV and/ or Transplant-related Diagnoses in Infants <1 Year of Age in the United States
by Patient and Hospital Characteristics, 1997–2009

Patient Characteristics	Infants <1 Year		P Value
	N (SE)	Rate per 100,000 (95% CI)	
Total overall	3734 (125)	18.6 (18.5, 18.7)	
Annual average	747 (26)		
Sex			0.001
Male	2010 (82)	19.6 (19.5, 19.7)	
Female	1723 (76)	17.6 (17.5, 17.7)	
Race/ethnicity*			0.001
White (non-Hispanic)	1312 (76)	11.5 (11.4, 11.6)	
Black (non-Hispanic)	697 (54)	23.5 (23.3, 23.6)	
Hispanic	596 (53)	13.0 (12.8, 13.2)	
Asian/Pacific Islander	111 (17)	12.1 (11.7, 12.5)	
Other	203 (24)	—	
Region			0.72
Northeast	582 (47)	17.3 (17.1, 17.4)	
Midwest	789 (71)	18.0 (17.8, 18.2)	
South	1575 (98)	21.2 (21.1, 21.3)	
West	788 (63)	16.0 (15.8, 16.2)	
Year			0.69
1997	763 (50)	20.3 (20.2, 20.4)	
2000	677 (58)	17.5 (17.3, 17.7)	
2003	700 (50)	17.3 (17.2, 17.4)	
2006	770 (50)	18.5 (18.4, 18.6)	
2009	823 (47)	19.3 (19.2, 19.4)	
Hospital characteristics	N (SE)	Proportion (%)	
Hospital type			
Urban teaching	2698 (117)	72.3	
Urban non-teaching	816 (40)	21.8	
Rural	109 (12)	2.9	
Hospital size			
Small	472 (53)	12.6	
Medium	888 (64)	23.8	
Large	2263 (96)	60.6	
Payment information			
Medicaid	2202 (89)	59.0	
Private/HMO	1214 (63)	32.5	

Patient Characteristics	Infants <1 Year		P Value
	N (SE)	Rate per 100,000 (95% CI)	
Self-pay	117 (17)	3.1	
Other	189 (28)	5.1	

Estimates were calculated using the KID dataset from the Healthcare Cost and Utilization Project.

* Information on race/ethnicity was missing for 21.2% of cCMV-related hospitalizations.

HMO indicates health maintenance organization.

Table 2
Medical Conditions and Procedures Identified Among Infants <1 Year of Age With
cCMV-related Hospitalizations Not Associated With HIV and/ or Transplant-related
Diagnoses in the United States, 1997–2009

	Congenital CMV-related Hospitalizations by Age Group			
	Infants <1 Month*		Infants <1 Year	
	N = 2042		N = 3734	
	N (SE)	%	N (SE)	%
cCMV-related conditions				
Thrombocytopenia	986 (45)	48.3	1495 (64)	40.0
Petechiae	87 (13)	4.3	136 (16)	3.6
Hepatomegaly	31 (7)	1.5	71 (11)	1.9
Splenomegaly	— [†]	— [†]	30 (9)	0.8
Microcephaly	149 (16)	7.3	384 (33)	10.3
Seizure	114 (22)	5.6	314 (34)	8.4
Other neurological symptoms	153 (18)	7.5	238 (24)	6.4
Hearing loss	82 (14)	4.0	247 (28)	6.6
Chorioretinitis	41 (10)	2.0	79 (14)	2.1
Any cCMV-related symptom	1233 (52)	60.4	2202 (89)	59.0
Other conditions				
Low birth weight	1185 (52)	58.0	1723 (73)	46.2
Jaundice	897 (46)	43.9	1287 (62)	34.5
Respiratory distress	1075 (51)	52.6	1766 (74)	47.3
Pneumonia	110 (18)	5.4	264 (28)	7.1
Reflux	69 (14)	3.4	277 (31)	7.4
Hydrocephalus	74 (13)	3.6	166 (21)	4.4
Failure to thrive	— [†]	— [†]	90 (16)	2.4
Died	88 (13)	4.3	157 (18)	4.2
Procedures				
Mechanical ventilation	743 (42)	36.4	1163 (57)	31.2
Transfusions	471 (35)	23.1	761 (48)	20.4
Feeding tubes	52 (12)	2.6	130 (18)	3.5

Estimates were calculated using the KID dataset from the Healthcare Cost and Utilization Project.

* Limited to data from hospitalizations among children with data on age in months. Age in months data was suppressed by some states.

[†] Estimated numbers with a relative SE >0.3 are considered less precise or unreliable measurements.