Early Childhood Outcomes of NICU Graduates with Cytomegalovirus Infection in California

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Abbreviations: CMV – cytomegalovirus, CPQCC – California Perinatal Quality Care Collaborative, HRIF – High-Risk Infant Follow-up, NICU – neonatal intensive care unit, VLBW – very low birth weight

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ABSTRACT

Background: To assess demographics and outcomes up to 3 years of age among children with cytomegalovirus (CMV) infection in California neonatal intensive care units (NICUs) during 2010–2021.

Methods: The California Perinatal Quality Care Collaborative (CPQCC) collects data on all very low birth weight (VLBW, birth weight ≤1500g) and acutely ill infants with birth weight >1500g across 92% of NICUs in California. VLBW infants and those with neurological conditions are referred to a statewide high-risk infant follow-up (HRIF) program. CMV infection was defined as a positive culture or PCR identified during the NICU hospitalization.

Results: During 2010–2021, CMV reporting rates averaged 3.5/1,000 VLBW infants (n=205) and 1.1/1,000 infants >1500g (n=128). Among all 333 infants with CMV, 314 (94%) were discharged home alive, 271 (86%) were referred for HRIF and 205 (65%) had ≥ 1 visit. Whereas infants born to mothers <20 years of age had highest CMV reporting rates and those born to Hispanic mothers comprised 49% of all infected infants, they had the highest loss of follow-up. At the 12-month visit (n=152), 19 (13%) infants with CMV had bilateral blindness and 18 (12%) had hearing loss. At the 24-month visit, 5 (5%) of 103 had severe cerebral palsy.

Conclusions: Among infants admitted to the NICU, those with CMV diagnoses may overrepresent infants with more severe CMV disease and outcomes. The CPQCC and HRIF program findings may help inform implementation of surveillance for congenital CMV infection in other U.S. states and guide strategies to reduce disparities in access to services. **Key Words:** cytomegalovirus, congenital infection, premature infant, very low birth weight infant, prevalence

Congenital cytomegalovirus (CMV) infection is the leading infectious cause of sensorineural hearing loss and developmental disabilities in U.S. children (2018). With a prevalence of 4.5 per 1,000 live births, up to 10% of infants with congenital CMV infection have been identified in the neonatal intensive care unit (NICU) (Fowler et al., 2017). Whereas postnatal CMV infection may cause severe disease (e.g., sepsis-like syndrome) and has been associated with a failed hearing screen in very low birth weight (VLBW) and premature infants, evidence of its association with poorer neurodevelopmental outcomes is not definitive (Gunkel et al., 2018; Turner et al., 2014; Weimer et al., 2020). Infants in the NICU are typically tested for CMV upon clinical suspicion (Tran et al., 2020). A reliable distinction between congenital and postnatal CMV infection requires laboratory testing on clinical specimens collected within 2–3 weeks of birth (Lazzarotto et al., 2008).

During 2005–2016, CMV infection, reported in 2.7/1,000 VLBW infants and 1.2/1,000 infants >1500g in California NICUs, was associated with longer hospital stay in both infant groups, and with increased mortality among infants >1500g (<u>Tran et al., 2020</u>). Early childhood outcomes of NICU graduates with CMV infection have not been assessed. A statewide high-risk infant follow-up (HRIF) program ensures that VLBW and other high-risk infants discharged from NICUs are monitored for growth and neurodevelopment outcomes through age 3 years to receive early intervention if subsequent complications are identified (<u>Pai et al., 2020</u>). In this study, we describe demographics, clinical characteristics, and outcomes up to 3 years of age among NICU graduates reported with CMV infection in California during 2010–2021.

Methods

We used linked data from the California Perinatal Quality Care Collaborative (CPQCC) and California Children's Service (CCS) HRIF program. CPQCC collects data for infants admitted to a member NICU at birth or within 28 days of life with one of the following eligibility criteria: a) birth weight between 401g–1500g; b) gestational age between 22 weeks–31 weeks 6 days at birth; or c) for infants with birth weight >1500g, either death, surgery, ventilation for >4 hours, severe hyperbilirubinemia, early bacterial sepsis, therapeutic hypothermia, or acute transfer. Trained NICU personnel conduct data abstraction using a standardized questionnaire which is electronically submitted. When appropriate, definitions align with those of the Vermont Oxford Network (2022b). Data include demographics, maternal and delivery history, post-delivery diagnoses and interventions (Tran et al., 2020).

The HRIF program provides a series of visits for eligible children through age 3 years (Pai et al., 2020). Infants who were cared for in a CCS-approved NICU with birth weight \leq 1500g, \leq 32 weeks gestational age, or birth weight >1500g, \geq 32 weeks gestational age with documented qualifying criteria are eligible for HRIF. Assigned personnel at the discharging NICU complete a web-based referral/registration form referring the infant to one of approximately 70 HRIF clinics across California. The statewide program includes 3 standard visits performed at approximately 4–8 months, 12–16 months, and 18–36 months (adjusted for chronological age) including comprehensive history, physical examination, neurological, developmental, psychosocial, hearing, and ophthalmologic assessments, and additional visits as deemed necessary. The CPQCC and HRIF databases are linked via a probabilistic linkage algorithm with >99% success (Pai et al., 2020).

VLBW infants and eligible infants >1500g admitted to CPQCC-member NICUs during 2010– 2021 were included in this study. The CPQCC NICU Admission/Discharge data collection form includes a specific field for recording congenital infections which include (but are not limited to) syphilis, toxoplasmosis, rubella, cytomegalovirus, and herpes simplex (2022a). A case of CMV infection is defined as a documented positive viral culture or polymerase chain reaction assay for CMV at any time since birth in an infant in the NICU. CMV laboratory testing is performed during diagnostic workup under the discretion of providers. However, data on specimen types or collection date are not recorded, precluding categorization of CMV cases as congenital or postnatal (Tran et al., 2020).

Among infants reported with CMV infection, we assessed the proportions with the following: small for gestational age (SGA), microcephaly, congenital anomalies, preterm morbidities, and neonatal death. SGA and microcephaly were defined as birth weight <10th percentile and birth head circumference <3rd percentile for their gestational age and gender, respectively, using the 2013 Fenton Preterm Growth Chart (Fenton and Kim, 2013). Among those who were discharged home alive, we assessed the proportions referred to the HRIF program and with at least one HRIF visit, by NICU care level, maternal age, maternal race or Hispanic origin, and health insurance type. We also assessed the median age at each standard visit, and the proportions of infants with CMV identified with visual impairment, hearing loss and interventions, neurological abnormalities, and cerebral palsy, among those seen at recommended ages 4–8 months, 12–16 months, and 18–36 months (adjusted for chronological age) for each standard follow-up visit.

We calculated reporting rates as the number of infants reported with CMV infection divided by the number of live births meeting CPQCC eligibility criteria, using binomial proportion and exact confidence intervals (CI). We assessed reporting rates by birth year, NICU care level, maternal age, and maternal race or Hispanic origin, separately for VLBW infants and infants >1500g. To compare reporting rates by subgroups, we estimated reporting rate ratios and 95% CI using a modified Poisson regression model with a robust error variance. We used SAS version 9.4 (SAS, Cary, NC) for all analyses.

Results

In CPQCC-member NICUs, 333 infants were reported with CMV infection during 2010–2021; 205 (62%) were VLBW infants and 128 (38%) were infants >1500g. During the 12-year period, CMV reporting rates averaged 3.5/1,000 VLBW infants and 1.1/1,000 infants >1500g. Among VLBW infants, reporting rates fluctuated between 2.2–4.9/1,000 with a decreasing trend during 2010–2016, increased from 3.5/1,000 in 2017 to 6.7/1,000 in 2020, and decreased to 1.8/1,000 in 2021 (Figure 1). Among infants >1500g, reporting rates ranged 0.3–1.7 per 1,000.

Most VLBW infants and infants >1500g with CMV infection were born at community or regional (i.e., tertiary) hospitals (Table 1). Among VLBW infants, there was no significant differences in reporting rates by maternal age, but infants born to Hispanic and Asian or Pacific Islanders mothers were approximately 2 times as likely to be reported with CMV infection as those born to Black mothers. In contrast, among infants >1500g, infants born to mothers <20 years of age were almost 3 times as likely to be reported with CMV infection as compared with infants born to mothers 20–29 years of age, but no significant differences by maternal race or Hispanic origin were found.

Clinical characteristics and in-hospital outcomes of infants with CMV infection are described in Table S1. Among 314 (94%) infants with CMV infection who were discharged home alive, 271 (86%) were referred to the HRIF program. The most common eligibility criteria for HRIF referral among infants with CMV infection was birth weight \leq 1500g (58%), gestational age <32 weeks (52%), neurological abnormalities (48%), and intracranial pathology with potential

adverse neurological outcome (25%). Overall, 205 (65%) infants had ≥ 1 follow-up visit, with the lowest proportions among infants born to mothers <20 years, of Hispanic origin , or without health insurance (Table S2). The proportion reported with visual impairment ranged from 7% to 14% between the first and second visit, respectively, and with hearing loss from 10% to 12% (Table 2). Among the 103 (38%) infants returning for a third visit, 6% were reported with moderate or severe cerebral palsy.

Discussion

We have used CPQCC data to describe trends in CMV infection among infants hospitalized in NICUs in California, identify groups at higher risk of disease, and describe outcomes up to 3 years of age among infants eligible for follow-up. During 2010–2021, CMV reporting rates averaged 3.5/1,000 VLBW infants and 1.1/1,000 infants >1500g, much lower than the prevalence of congenital CMV infection among infants in the NICU (13.9 per 1,000) estimated in a large newborn screening study in the United States (Fowler et al., 2017). Considering data since 2005 (Tran et al., 2020), CMV reporting rates among VLBW infants increased over time, reaching 6.7/1,000 in 2020, and was stable (range: 0.7–1.5/1,000) among infants >1500g. Data from VLBW infants are nearly population-based, though generalizability of the findings for the infants >1500g is less clear, as data collection for that subgroup is limited to those with certain eligibility criteria. Of note, CMV reporting rates among VLBW infants decreased to 1.8/1,000 in 2021, consistent with findings of a newborn screening study in Minnesota which documented a 70% reduction in congenital CMV prevalence during the COVID-19 pandemic (Schleiss et al., 2022). It is possible that testing practices among VLBW infants have changed due to increased awareness of both congenital CMV infection and risk of postnatal CMV infection through human milk feeding (Lanzieri et al., 2013). We have found that ~50% of CPQCC-member

NICUs had quality improvement projects on human milk feeding during 2010–2021 but no project specifically mentioning CMV prevention or testing (2023).

CMV reporting rate among infants >1500g was highest among infants born to mothers ≤ 20 years of age. Among VLBW infants, we observed higher reporting rates among those born to Hispanic mothers and Asian or Pacific Islander mothers. Although our study does not distinguish congenital from postnatal infection, unpublished national data indicate ~90% of infants tested for CMV in the NICU had specimens collected within 21 days of life (Raines et al., 2023). A prior study in California noted higher prevalence of congenital CMV infection among infants born to Hispanic and Black mothers (Kharrazi et al., 2010). More recent newborn screening studies in other regions of the United States have shown a lower prevalence among Hispanic infants compared to White infants, and either higher or similar prevalence among Black infants (Fowler et al., 2018; Schleiss et al., 2022). Maternal CMV seroprevalence among Hispanic and Asian individuals in California is nearly 90% (Kharrazi et al., 2010), which increases the risk of postnatal CMV infection through breastmilk feeding. In addition, among infants referred to follow-up, the proportion with ≥ 1 visit varied with maternal age, race or Hispanic origin and health insurance support. Prior analysis of CPQCC and HRIF data revealed racial disparities on referral rates among VLBW infants, which lessened following implementation of a state-wide initiative in 2013 to address disparities in referrals (Pai et al., 2020). Identifying groups at higher risk of CMV infection and loss of follow-up may help guide strategies to prevent CMV infection and to reduce disparities in access to services.

This study has several limitations. First, date of specimen collection for CMV testing to distinguish congenital from postnatal infection, and data on most clinical signs of congenital CMV at birth or antiviral treatment were not captured. Second, cases identified in NICUs would

overrepresent infants with more severe disease and outcomes in comparison to those that would be identified by newborn screening, 90% of whom have no clinical signs at birth. For example, 19%–27% of infants with CMV infection had microcephaly, a greater proportion than observed in cohorts of >50 infants with congenital CMV infection identified through newborn screening (0.8–2.5%) (Ahlfors et al., 1999; Boppana et al., 1999; Koyano et al., 2011; Peckham et al., 1983; Saigal et al., 1982; Yamamoto et al., 2011). Third, not all infants referred to the HRIF program returned for any or all of the 3 standard visits at the time of this analysis, either due to loss of follow-up (37%) or for being too young (25%). By the second follow-up visit, at median age 13 months, 14% of infants with CMV infection enrolled in the HRIF program had visual impairment, 12% had hearing loss and 38% suspected or confirmed neurological problems, which may or may not be attributed to CMV infection. Loss to follow up is unlikely to be random, and children with neurodevelopment concerns may have been more likely to return for visits. However, this study was descriptive in nature and did not include comparisons of outcomes among infants without reported CMV infection.

Among infants admitted to the NICU, those with CMV diagnoses may overrepresent infants with more severe CMV disease and outcomes. We found increased reporting of CMV infection among VLBW infants within NICUs in California during 2010–2021. Surveillance for congenital CMV is not conducted in California; thus, these data have been useful to monitor trends in CMV infection among NICU infants and describe clinical outcomes in a subset of infants who were eligible for the HRIF program. The work from the CPQCC and HRIF program may be informative to the wider implementation of congenital CMV surveillance efforts by health departments. Only 10 U.S. states conduct congenital CMV surveillance and case definitions are not standardized (Raines et al., 2022). Collecting data on clinical signs at birth,

laboratory results, including specimen type, age at specimen collection, and testing methods, and outcomes such as hearing loss, would be important to accurately classify cases of congenital CMV and document the disease burden.

References

- Department of Health Care Services. California Children's Services. High Risk Infant Follow-Up Program Letter. October 12, 2016.
- 2018. American Academy of Pediatrics. Cytomegalovirus Infection. In: Kimberlin D.W., Brady MT, Jackson MA, Long SS, eds. Red Book: 2018 Report of the Committee on Infectious Diseases. 31st ed Itasca, IL: American Academy of Pediatrics.
- 2022a. California Perinatal Quality Care Collaborative. NICU Data Manual of Definitions. .
- 2022b. Vermont Oxford Network. Databases and Reporting. .
- 2023. California Perinatal Quality Care Collaborative. Quality Improvement Projects.
- Ahlfors K, Ivarsson SA, Harris S. 1999. Report on a long-term study of maternal and congenital cytomegalovirus infection in Sweden. Review of prospective studies available in the literature. Scand J Infect Dis 31(5):443-457.
- Boppana SB, Fowler KB, Britt WJ, Stagno S, Pass RF. 1999. Symptomatic congenital cytomegalovirus infection in infants born to mothers with preexisting immunity to cytomegalovirus. Pediatrics 104(1 Pt 1):55-60.
- Fenton TR, Kim JH. 2013. A systematic review and meta-analysis to revise the Fenton growth chart for preterm infants. BMC Pediatr 13:59.
- Fowler KB, McCollister FP, Sabo DL, Shoup AG, Owen KE, Woodruff JL, Cox E, Mohamed LS, Choo DI, Boppana SB, Study C. 2017. A Targeted Approach for Congenital Cytomegalovirus Screening Within Newborn Hearing Screening. Pediatrics 139(2).
- Fowler KB, Ross SA, Shimamura M, Ahmed A, Palmer AL, Michaels MG, Bernstein DI,
 Sanchez PJ, Feja KN, Stewart A, Boppana S. 2018. Racial and Ethnic Differences in the
 Prevalence of Congenital Cytomegalovirus Infection. J Pediatr 200:196-201 e191.

- Gunkel J, de Vries LS, Jongmans M, Koopman-Esseboom C, van Haastert IC, Eijsermans MCJ, van Stam C, van Zanten BGA, Wolfs TFW, Nijman J. 2018. Outcome of Preterm Infants With Postnatal Cytomegalovirus Infection. Pediatrics 141(2).
- Kharrazi M, Hyde T, Young S, Amin MM, Cannon MJ, Dollard SC. 2010. Use of screening dried blood spots for estimation of prevalence, risk factors, and birth outcomes of congenital cytomegalovirus infection. J Pediatr 157(2):191-197.
- Koyano S, Inoue N, Oka A, Moriuchi H, Asano K, Ito Y, Yamada H, Yoshikawa T, Suzutani T, Japanese Congenital Cytomegalovirus Study G. 2011. Screening for congenital cytomegalovirus infection using newborn urine samples collected on filter paper: feasibility and outcomes from a multicentre study. BMJ Open 1(1):e000118.
- Lanzieri TM, Dollard SC, Josephson CD, Schmid DS, Bialek SR. 2013. Breast milk-acquired cytomegalovirus infection and disease in VLBW and premature infants. Pediatrics 131(6):e1937-1945.
- Lazzarotto T, Guerra B, Lanari M, Gabrielli L, Landini MP. 2008. New advances in the diagnosis of congenital cytomegalovirus infection. J Clin Virol 41(3):192-197.
- Pai VV, Kan P, Bennett M, Carmichael SL, Lee HC, Hintz SR. 2020. Improved Referral of Very Low Birthweight Infants to High-Risk Infant Follow-Up in California. J Pediatr 216:101-108 e101.
- Peckham CS, Chin KS, Coleman JC, Henderson K, Hurley R, Preece PM. 1983.Cytomegalovirus infection in pregnancy: preliminary findings from a prospective study.Lancet 1(8338):1352-1355.
- Raines K, Heitman KN, Leung J, Woodworth KR, Tong VT, Sugerman DE, Lanzieri TM. 2022. Congenital cytomegalovirus surveillance in the United States. Birth Defects Res.

- Raines K, Rau A, Clark RH, Sugerman DE, Lanzieri TM. 2023. Congenital cytomegalovirus among infants in U.S. neonatal intensive care units during 2010-2020. Abstract submitted to the 2023 Congenital Cytomegalovirus Public Health and Policy Conference.
- Saigal S, Lunyk O, Larke RP, Chernesky MA. 1982. The outcome in children with congenital cytomegalovirus infection. A longitudinal follow-up study. Am J Dis Child 136(10):896-901.
- Schleiss MR, Rosendahl S, McCann M, Dollard SC, Lanzieri TM. 2022. Assessment of Congenital Cytomegalovirus Prevalence Among Newborns in Minnesota During the COVID-19 Pandemic. JAMA Netw Open 5(9):e2230020.
- Tran C, Bennett MV, Gould JB, Lee HC, Lanzieri TM. 2020. Cytomegalovirus Infection among Infants in Neonatal Intensive Care Units, California, 2005 to 2016. Am J Perinatol 37(2):146-150.
- Turner KM, Lee HC, Boppana SB, Carlo WA, Randolph DA. 2014. Incidence and impact of CMV infection in very low birth weight infants. Pediatrics 133(3):e609-615.
- Weimer KED, Kelly MS, Permar SR, Clark RH, Greenberg RG. 2020. Association of Adverse Hearing, Growth, and Discharge Age Outcomes With Postnatal Cytomegalovirus Infection in Infants With Very Low Birth Weight. JAMA Pediatr 174(2):133-140.
- Yamamoto AY, Mussi-Pinhata MM, Isaac Mde L, Amaral FR, Carvalheiro CG, Aragon DC, Manfredi AK, Boppana SB, Britt WJ. 2011. Congenital cytomegalovirus infection as a cause of sensorineural hearing loss in a highly immune population. Pediatr Infect Dis J 30(12):1043-1046.

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TABLES AND FIGURES

Table 1. NICU level and maternal demographics of infants with CMV infection reported among VLBW infants and infants >1500g in California NICUs, 2010–2021

Table 2. Outcomes of infants reported with CMV infection enrolled in the high-risk infant follow-up program in California, 2010-2021

Figure 1. Number of VLBW infants and infants >1500g with CMV infection and CMV reporting rates in NICUs, California, 2010–2021 Caption: Dashed and solid lines represent reporting rates for VLBW infants and infants >1500g, respectively.

Supplementary material

Table S1. Clinical characteristics and in-hospital outcomes of infants reported with CMV infection in California, 2010-2021

Table S2. Characteristics of infants with CMV infection discharged home alive, referred to the high-risk infant follow-up program and with at least one follow-up visit, California, 2010-2021

CPQCC-member NICUs, California, 2010-2021

	VLBW infants			Infants >1500g		
	reported with	CMV reporting		reported with	CMV	
	CMV infection	rate		CMV infection	reporting	
	n (%)	per 1,000	Rate ratio	n (%)	per 1,000	Rate ratio
Characteristic	n=205	(95% CI)	(95% CI)	n=128	(95% CI)	(95% CI)
Birth hospital level (NICU level) ^a						
Intermediate (II)	1 (0.5)	0.9 (0.0-4.9)	0.3 (0.0–1.9)	5 (3.9)	2.1 (0.8–1.3)	1.9 (0.8–4.8)
Community (IIIA/B)	115 (56.1)	3.5 (2.9–4.2)	Reference	52 (40.6)	1.1 (0.8–1.4)	Reference
Regional (IIIC/D)	86 (42.0)	4.1 (3.3–5.0)	1.2 (0.0–1.9)	67 (52.3)	1.0 (0.8–1.3)	1.0 (0.7–1.4)
Non-CCS	3 (1.5)	1.2 (0.2–3.4)	0.3 (0.1–1.1)	4 (3.1)	1.0 (0.3–2.4)	0.9 (0.3–2.5)
Maternal age, years						
<20	16 (7.8)	4.8 (2.7–7.7)	1.4 (0.8-2.4)	21 (16.4)	3.0 (1.96)	2.5 (1.5-4.1)
20-29	80 (39.0)	3.5 (2.8-4.3)	Reference	61 (47.7)	1.2 (0.9–1.5)	Reference
30-39	94 (45.9)	3.4 (2.8–4.2)	1.0 (0.7–1.3)	38 (29.7)	0.7 (0.5–1.0)	0.6 (0.4–0.9)
≥40	15 (7.3)	3.6 (2.0-5.9)	1.0 (0.6–1.8)	7 (5.5)	1.0 (0.4–2.0)	0.8 (0.4–1.8)
Maternal race or Hispanic origin						
Hispanic ^b	105 (51.2)	4.1 (3.3–4.9)	1.9 (1.1–3.1)	59 (46.1)	1.1 (0.8–1.4)	0.7 (0.4–1.2)
Non-Hispanic						
Black	17 (8.3)	2.2 (1.3-3.5)	Reference	15 (11.7)	1.6 (0.9–2.7)	Reference
White	36 (17.6)	2.5 (1.7–3.4)	1.1 (0.6–2.0)	40 (31.3)	1.0 (0.7–1.4)	0.6 (0.4–1.1)
Asian or Pacific Islander	38 (18.5)	5.0 (3.5-6.8)	2.3 (1.3-4.0)	9 (7.0)	0.7 (0.3–1.4)	0.4 (0.2–1.1)
American Indian, Alaska Native or Other	8 (3.9)	4.2 (1.8-8.2)	1.9 (0.8–4.4)	4 (0.0)	0.9 (0.3–2.3)	0.6 (0.2–1.7)

^a NICUs were categorized into 3 levels (intermediate, community, and regional) based on CCS guidelines, American Academy of Pediatrics designation, and the services provided at each NICU. NICUs that choose not to participate in the CCS program were defined as non-CCS.

^bHispanic includes all Hispanics regardless of race.

CCS: California Children's Service

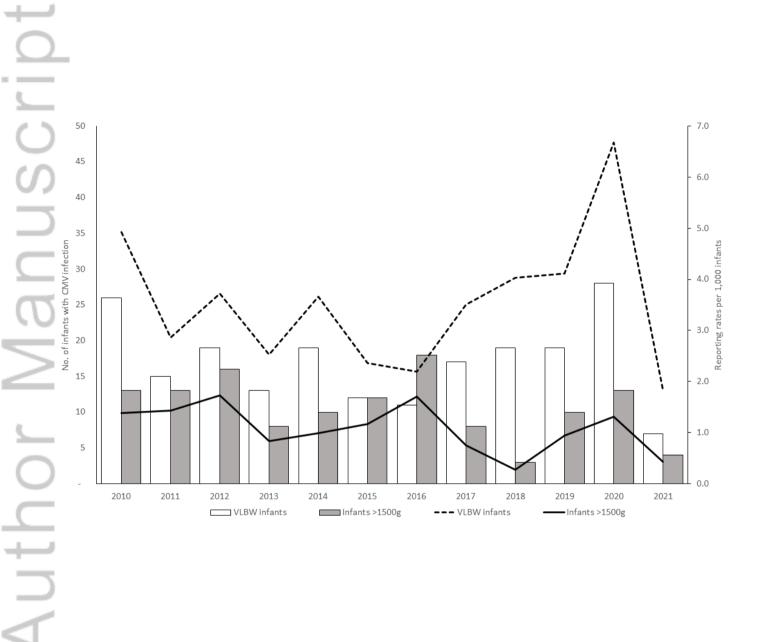
Table 2. Outcomes of infants reported with CMV infection enrolled in the high-risk infant
follow-up program in California, 2010-2021

	No. (%) of infants with CMV infection ^a						
	First Visit (4-8 months) n=205		Secon	Second Visit		Third Visit	
				months)		months)	
Outcomes			n=	152	n=	n=103	
Visual impairment							
Yes	14	(7)	22	(14)	11	(11)	
No	174	(85)	122	(80)	87	(84)	
Unknown	17	(8)	8	(5)	5	(5)	
Blindness							
Bilateral	9	(4)	19	(13)	9	(9)	
Unilateral	3	(1)	3	(2)	1	(1)	
Unknown	1	(0)	0	(0)	1	(1)	
Hearing loss							
Yes	21	(10)	18	(12)	6	(6)	
No	165	(80)	116	(76)	84	(82)	
Unknown	5	(2)	6	(4)	6	(6)	
Assessment in progress	14	(7)	12	(8)	7	(7)	
Hearing loss (laterality)							
Bilateral	10	(5)	9	(6)	4	(4)	
Unilateral	10	(5)	9	(6)	1	(1)	
Assessment in progress	0	(0)	0	(0)	1	(1)	
Unknown	1	(0)	0	(0)	0	(0)	
Assisted listening device							
Yes, recommended and received	9	(4)	10	(7)	5	(5)	
Yes, recommended but not received	6	(3)	2	(1)	0	(0)	
No	6	(3)	5	(3)	1	(1)	
Unknown	0	(0)	1	(1)	0	(0)	
Type of assisted listening device							
Cochlear implant	1	(0)	0	(0)	0	(0)	
Hearing aid	11		9	(6)	5	(5)	
Unknown	2	(1)	4	(3)	0	(0)	
Neurological status							
Abnormal or suspect	87	(42)	58	(38)	31	(30)	
Normal	105	(51)	85	(56)	66	(64)	
N/A	13	(6)	9	(6)	6	(6)	
Cerebral palsy status (18-36 months)							
Mild – GMFCS level I			0	(0)	0	(0)	
Moderate – GMFCS level II to III			2	(1)	1	(1)	

Severe – GMFCS level IV to V	3	(2)	5	(5)
Unable to determine	3	(2)	2	(2)
No	35	(23)	93	(90)
N/A	109	(72)	1	(1)
Autism spectrum screen (18 months)				
Not pass			12	(12)
Pass			40	(39)
Referred for further autism spectrum assessment				
Yes			6	(6)
No			45	(44)

^a Proportions of infants with CMV identified with an outcome among those seen at recommended ages 4–8 months, 12–16 months, and 18–36 months (adjusted for chronological age) for each standard follow-up visit. The median age (interquartile range) was 6 (5-7) months for the first visit, 13 (12-16) months for the second visit, and 26 (23-29) months for the third visit.

GMFCS: Gross Motor Function Classification System. Level I: has functional gross motor skills, though may struggle with speed, balance, and coordination; moves independently without the aid of adaptive equipment. Level II: can walk with limitations and may need assistance with inclined or uneven surfaces; moves without the aid of adaptive equipment. Level III: can walk with the use of hand-held adaptive equipment and may need a wheelchair to move on inclined or uneven surfaces, or to travel long distances. Level IV: is self-mobile only with significant limitations; many use powered wheelchairs, require significant help with transfers, and are dependent on adaptive and assistive equipment. Level V: typically has limitations that impair all voluntary movement and is extremely dependent on adaptive equipment, assistive technology, and other people for mobility.



CPQCC-member NICUs, California, 2010–2021

	VLBW infants			Infants >1500g		
	reported with	CMV reporting		reported with	CMV	
	CMV infection	rate		CMV infection	reporting	
	n (%)	per 1,000	Rate ratio	n (%)	per 1,000	Rate ratio
Characteristic	n=205	(95% CI)	(95% CI)	n=128	(95% CI)	(95% CI)
Birth hospital level (NICU level) ^a						
Intermediate (II)	1 (0.5)	0.9 (0.0-4.9)	0.3 (0.0–1.9)	5 (3.9)	2.1 (0.8–1.3)	1.9 (0.8–4.8)
Community (IIIA/B)	115 (56.1)	3.5 (2.9–4.2)	Reference	52 (40.6)	1.1 (0.8–1.4)	Reference
Regional (IIIC/D)	86 (42.0)	4.1 (3.3–5.0)	1.2 (0.0–1.9)	67 (52.3)	1.0 (0.8–1.3)	1.0 (0.7–1.4)
Non-CCS	3 (1.5)	1.2 (0.2–3.4)	0.3 (0.1–1.1)	4 (3.1)	1.0 (0.3–2.4)	0.9 (0.3–2.5)
Maternal age, years						
<20	16 (7.8)	4.8 (2.7–7.7)	1.4 (0.8-2.4)	21 (16.4)	3.0 (1.96)	2.5 (1.5-4.1)
20-29	80 (39.0)	3.5 (2.8–4.3)	Reference	61 (47.7)	1.2 (0.9–1.5)	Reference
30-39	94 (45.9)	3.4 (2.8–4.2)	1.0 (0.7–1.3)	38 (29.7)	0.7 (0.5–1.0)	0.6 (0.4–0.9)
≥40	15 (7.3)	3.6 (2.0-5.9)	1.0 (0.6–1.8)	7 (5.5)	1.0 (0.4–2.0)	0.8 (0.4–1.8)
Maternal race or Hispanic origin						
Hispanic ^b	105 (51.2)	4.1 (3.3–4.9)	1.9 (1.1–3.1)	59 (46.1)	1.1 (0.8–1.4)	0.7 (0.4–1.2)
Non-Hispanic						
Black	17 (8.3)	2.2 (1.3-3.5)	Reference	15 (11.7)	1.6 (0.9–2.7)	Reference
White	36 (17.6)	2.5 (1.7–3.4)	1.1 (0.6–2.0)	40 (31.3)	1.0 (0.7–1.4)	0.6 (0.4–1.1)
Asian or Pacific Islander	38 (18.5)	5.0 (3.5-6.8)	2.3 (1.3-4.0)	9 (7.0)	0.7 (0.3–1.4)	0.4 (0.2–1.1)
American Indian, Alaska Native or Other	8 (3.9)	4.2 (1.8-8.2)	1.9 (0.8–4.4)	4 (0.0)	0.9 (0.3–2.3)	0.6 (0.2–1.7)

^a NICUs were categorized into 3 levels (intermediate, community, and regional) based on CCS guidelines, American Academy of Pediatrics designation, and the services provided at each NICU. NICUs that choose not to participate in the CCS program were defined as non-CCS.

^bHispanic includes all Hispanics regardless of race.

CCS: California Children's Service

Table 2. Outcomes of infants reported with CMV infection enrolled in the high-risk infantfollow-up program in California, 2010-2021

	No. (%) of infants with CMV infection ^a						
	First Visit (4-8 months) n=205		Secon	d Visit months)	Third Visit (18-36 months) n=103		
Outcomes				152			
Outcomes Visual impairment				132			
•	14	(7)	22	(14)	11	(11)	
Yes	14	(7)	22	(14)	11	(11)	
No	174	(85)	122	(80)	87	(84)	
Unknown	17	(8)	8	(5)	5	(5)	
Blindness	0		10	(10)	0		
Bilateral	9	(4)	19	(13)	9	(9)	
Unilateral	3	(1)	3	(2)	1	(1)	
Unknown	1	(0)	0	(0)	1	(1)	
Hearing loss							
Yes	21	(10)	18	(12)	6	(6)	
No	165	(80)	116	(76)	84	(82)	
Unknown	5	(2)	6	(4)	6	(6)	
Assessment in progress	14	(7)	12	(8)	7	(7)	
Hearing loss (laterality)							
Bilateral	10	(5)	9	(6)	4	(4)	
Unilateral	10	(5)	9	(6)	1	(1)	
Assessment in progress	0	(0)	0	(0)	1	(1)	
Unknown	1	(0)	0	(0)	0	(0)	
Assisted listening device							
Yes, recommended and received	9	(4)	10	(7)	5	(5)	
Yes, recommended but not received	6	(3)	2	(1)	0	(0)	
No	6	(3)	5	(3)	1	(1)	
Unknown	0	(0)	1	(1)	0	(0)	
Type of assisted listening device							
Cochlear implant	1	(0)	0	(0)	0	(0)	
Hearing aid	11	(5)	9	(6)	5	(5)	
Unknown	2	(1)	4	(3)	0	(0)	
Neurological status							
Abnormal or suspect	87	(42)	58	(38)	31	(30)	
Normal	105	(51)	85	(56)	66	(64)	
N/A	13	(6)	9	(6)	6	(6)	
Cerebral palsy status (18-36 months)				2			
Mild – GMFCS level I			0	(0)	0	(0)	
Moderate – GMFCS level II to III			2	(1)	1	(1)	
Severe – GMFCS level IV to V			3	(2)	5	(5)	

Unable to determine	3	(2)	2	(2)
No	35	(23)	93	(90)
N/A	109	(72)	1	(1)
Autism spectrum screen (18 months)				
Not pass			12	(12)
Pass			40	(39)
Referred for further autism spectrum assessment				
Yes			6	(6)
No			45	(44)

^a Proportions of infants with CMV identified with an outcome among those seen at recommended ages 4–8 months, 12–16 months, and 18–36 months (adjusted for chronological age) for each standard follow-up visit. The median age (interquartile range) was 6 (5-7) months for the first visit, 13 (12-16) months for the second visit, and 26 (23-29) months for the third visit.

GMFCS: Gross Motor Function Classification System. Level I: has functional gross motor skills, though may struggle with speed, balance, and coordination; moves independently without the aid of adaptive equipment. Level II: can walk with limitations and may need assistance with inclined or uneven surfaces; moves without the aid of adaptive equipment. Level III: can walk with the use of hand-held adaptive equipment and may need a wheelchair to move on inclined or uneven surfaces, or to travel long distances. Level IV: is self-mobile only with significant limitations; many use powered wheelchairs, require significant help with transfers, and are dependent on adaptive and assistive equipment. Level V: typically has limitations that impair all voluntary movement and is extremely dependent on adaptive equipment, assistive technology, and other people for mobility.