Economic Burden of Congenital Cytomegalovirus Infection in Commercially- and Medicaid-Insured Patients in the United States

- cCMV is the leading infectious cause of congenital birth defects and neurological disabilities,¹⁻³ and approximately 20%-25% of infants with cCMV develop symptoms or long-term health complications including hearing loss, microcephaly, and developmental issues.^{1,4}
- Despite the risk of serious health complications, cCMV is difficult to diagnose because only 10%-15% of infants with cCMV display symptoms at birth.^{1,5,8-9} An additional challenge is the lack of systematic surveillance for cCMV.
- Although cCMV can result in serious health-related complications in the short- and long-term, the few published studies on the economic burden in the United States are limited.¹⁰⁻¹³

• This analysis aimed to assess healthcare resource utilization (HRU) and cost burden among samples of commerciallyand Medicaid-insured patients with cCMV in the United States using health insurance claims data.

PATIENTS AND METHODS

Data sources and cohort selection

- Health insurance claims data from January 1, 2010 through December 31, 2019 from the IBM Watson Health MarketScan® Commercial Claims and Encounters and Multi-State Medicaid databases were analyzed retrospectively. - Patients were included in either the commercially- or Medicaid-insured population.
- Patients with ≥1 diagnosis code for birth in their medical claims (ICD-9: V29-V39; ICD-10: Z38, Z05) or in their mother's linked medical claims (ICD-9: V27; ICD-10: Z37) were included.
- DOB for patients was defined as the earliest of the first claim for birth in the child's medical claims and the mid-point of the mother's birth admission.
- Patients were included in the cCMV cohort ("cases") if they had ≥1 diagnosis code for cCMV (ICD-9: 771.1; ICD-10: P35.1) or CMV (ICD-9: 078.5; ICD-10: B25) on a claim during the month following birth.
- All patients were required to have continuous enrollment for ≥1 year following the index date.
- The index date was defined as the first diagnosis of cCMV in the data for cases vs. selected at random from all medical claims within 1 month of birth for non-cCMV controls.
- cCMV cases were matched 1:1 to non-cCMV controls on demographic characteristics, health insurance type, birth year, and year of index date.
- Patients were followed for one-year post-index date (study period).

Figure 1. Identification of commercially- and Medicaid-insured cCMV patients.

≥1 diagnosis code for cCMV or CMV within 1 month of birth, on a claim between January 1, 2010 and December 31, 2019				
N (Medicaid) = 886	N (Commercial) = 491			
≥1 year continuous eligibility following index date				
N (Medicaid) = 554	N (Commercial) = 195			
Matched 1:1 to non-cCMV control				
N (Medicaid) = 549	N (Commercial) = 195			
cCMV, congenital cytomegalovirus; CMV, cytomegalovirus.				

Study outcomes

• All-cause HRU and costs were assessed throughout the one-year study period (including 3-month time periods).

- The HRU categories assessed included: all visits; inpatient admissions; emergency department (ED) visits; outpatient
- visits; and lab/imaging visits.
- » Lab/imaging visits were a subset of outpatient visits.
- » Inpatient admissions excluded admissions associated with birth, which were described separately.
- All-cause costs were reported in 2021 US dollars (\$).
- For each type of visit, values were reported as the average total number of visits and average total costs per patient among patients with ≥ 1 visit during the study period.
- Length of stay (LOS) and costs associated with birth admissions were described separately.
- Birth admission was defined as the inpatient admission during which the patient was born. Only patients whose birth was captured in their claims during an inpatient admission were included.
- » Birth admission LOS and costs were summarized over the entire inpatient admission during which the patient was born. • Select cCMV-related sequelae were assessed over the study period and reported as the proportion of patients with the sequelae.
- Comparisons between the matched case and control cohorts were conducted using Wilcoxon sign-rank test for continuous variables and McNemar's tests for categorical variables.

populations.

HMO, health maintenance organization; POS, point-of-service; SD, standard deviation. **Note:** Cases and controls were matched 1:1 on the above patient characteristics. Within each payer population, the values are the same among case and control populations.

- (Figure 3).
- (Figure 3).

All-cause costs

- (Table 3)

John Diaz-Decaro¹, Gail J. Demmler-Harrison², Jessica R. Marden³, Annika Anderson⁴, Sandeep Basnet¹, Katherine Gaburo³, Danielle Peterson³, Kosuke Kawai¹, Noam Kirson³, Urvi Desai³, Philip Buck¹ ¹Moderna, Inc., Cambridge, MA, United States, ²Baylor College of Medicine, Pediatric Infectious Disease, Texas Children's Hospital, Houston, TX, United States, ³Analysis Group, Inc., Boston, MA, United States, ⁴Analysis Group, Inc., New York, NY, United States

RESULTS

Patient characteristics

This analysis included 195 commercially-insured and 549 Medicaid-insured matched pairs.

Patient characteristics on the index date for the commercially- and Medicaid-insured populations are shown in **Table 1**.

Table 1. Patient characteristics for commercially- and Medicaid-insured

Patient characteristics at the index date	Commercially-insured population (N = 195 matched pairs)	Medicaid-insured population (N = 549 matched pairs)			
Age (months), mean ± SD	0.3 ± 0.3	0.2 ± 0.3			
Age (days), mean ± SD	8.4 ± 8.6	5.9 ± 7.8			
Male	96 (49.2%)	304 (55.4%)			
Insurance type					
HMO	29 (14.9%)	386 (70.3%)			
POS	23 (11.8%)	1 (0.2%)			
Non-HMO/POS	143 (73.3%)	162 (29.5%)			

All-cause HRU

Throughout the study period, 194 commercially-insured cases and 195 controls experienced a mean \pm SD number of 30.0 \pm 25.0 and 13.8 \pm 8.3 medical visits, respectively (Figure 2); 543 Medicaid-insured cases and controls experience a mean \pm SD number of 29.0 \pm 79.7 and 12.3 \pm 7.6 medical visits, respectively

During the study period, commercially-insured cases experienced a mean ± SD of 1.3 ± 0.7 inpatient visits with a mean \pm SD inpatient LOS of 19.4 ± 46.8 days, compared to 1.1 ± 0.3 inpatient admissions with a LOS of 3.2 ± 2.6 days among controls (p<.05) (**Figure 2**).

Medicaid-insured cases experienced a mean ± SD of 1.7 ± 1.5 inpatient visits with a mean \pm SD inpatient LOS of 16.3 \pm 25.5 days, compared to 1.1 \pm 0.3 inpatient admissions with a LOS of 7.6 ± 15.2 days among controls (p<.01)

Average birth admission duration for cases (vs. controls) was 23.7 days (vs. 5.1 days) among commercially-insured patients, and 24.0 days (vs. 5.2 days) among Medicaid-insured.

Mean ± SD total medical costs during the study period among commercially-insured patients were \$38,742 ± \$161,537 among cases and \$5,519 ± \$6,813 among controls (**Table 2**).

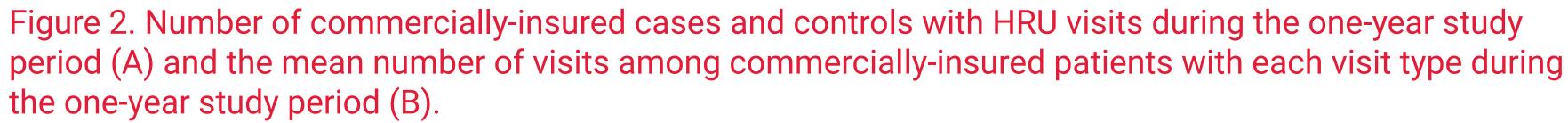
 Costs among cases peaked in the first three months of the study period (\$13,545 ± \$66,160), driven by costly inpatient admissions (\$58,521 ± \$148,195), and remained high through the year. (Table 2).

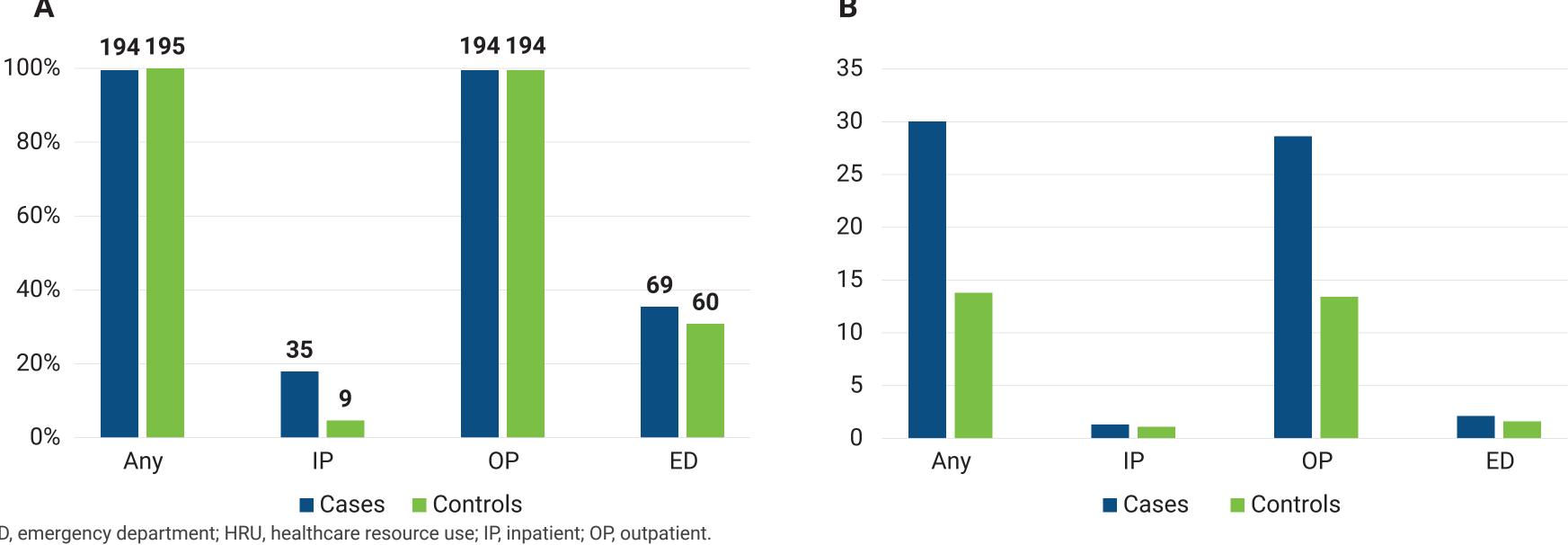
- Mean birth admission costs were summarized separately, and were \$149,192 for cases and \$17,996 for controls.

Average total medical costs during the study period among Medicaid-insured cases and controls were \$13,212 ± \$45,789 and \$3,464 ± \$21,677, respectively

 Mean medical costs among cases were highest in the 3–6-month period due to higher costs associated with inpatient admissions (\$15,553). (**Table 3**). - Mean birth admission costs were \$49,885 and \$5,052 for cases and controls, respectively.

During the study period, mean ± SD pharmacy costs for commercially- and Medicaid-insured patients were \$3,019 ± \$7,862 for cases (vs. \$330 ± \$2,494 for controls) and \$2,353 ± \$4,809 (vs. \$360 ± \$2,147), respectively.





ED, emergency department: HRU, healthcare resource use: IP, inpatient: OP, outpatient Note: Lab/imaging visits were a subset of outpatient visits. During the one-year study period, 168 (86.2%) case patients experienced a mean number of 6.6 lab/imaging visits and 149 (76.4%) control patients experienced an average of 2.4 lab/imaging visits.

Table 2. All-cause healthcare costs among commercially-insured patients during the 1-year study period.

		Year 1		
All-cause costs ^{1,2}	Cases N = 195	Controls N = 195	P-value	
<mark>Medical costs</mark> Mean ± SD Median [IQR]	\$38,742 ± \$161,537 \$9,075 [\$3,902 - \$22,172]	\$5,519 ± \$6,813 \$3,310 [\$2,554 - \$5,334]	0.005	
Inpatient costs Mean ± SD Median [IQR]	\$121,981 ± \$351,560 \$21,036 [\$9,595 - \$60,106]	\$12,921 ± \$10,357 \$9,858 [\$7,679 - \$17,263]	0.076	
Outpatient costs Mean ± SD Median [IQR]	\$15,451 ± \$31,052 \$6,615 [\$3,318 - \$13,255]	\$4,358 ± \$4,875 \$3,094 [\$2,488 - \$4,371]	<.0001	
Lab/imaging costs Mean ± SD Median [IQR]	\$1,662 ± \$2,927 \$548 [\$92 - \$2,356]	\$302 ± \$883 \$32 [\$11 - \$203]	<.0001	
ED costs Mean ± SD Median [IQR]	\$1,944 ± \$3,039 \$1,081 [\$319 - \$2,449]	\$1,708 ± \$3,749 \$564 [\$142 - \$1,435]	0.693	
Pharmacy costs Mean ± SD Median [IQR]	\$3,019 ± \$7,862 \$283 [\$30 - \$3,053]	\$330 ± \$2,494 \$23 [\$0 - \$107]	<.0001	

[1] Costs were summarized only among patients with that type of HRU during the study period. [2] Costs were measured from the payer perspective and adjusted to 2021 USD (\$).

Commonly-observed sequelae

- The most common sequelae during the study period among commercially-insured cases (vs. controls) were hearing loss (38.5% [vs. 3.1%]), developmental and motor delays (17.9% [vs. 2.6%]), liver-related conditions (17.9% [vs. 16.9%]), and vision loss (17.4% [vs. 1.5%]) (**Figure 4**).
- Among Medicaid-insured cases (vs. controls), the most common sequelae during the study period were hearing loss (29.1% [vs. 1.8%]), developmental and motor delays (22.0% [vs. 2.6%]), congenital malformations of the nervous system (18.2% [vs. 1.3%]), and cardiovascular disease (14.9% [vs. 1.8%]) (**Figure 5**).

Figure 4. Commonly-observed sequelae among commercially-insured patients during the 1-year study period.

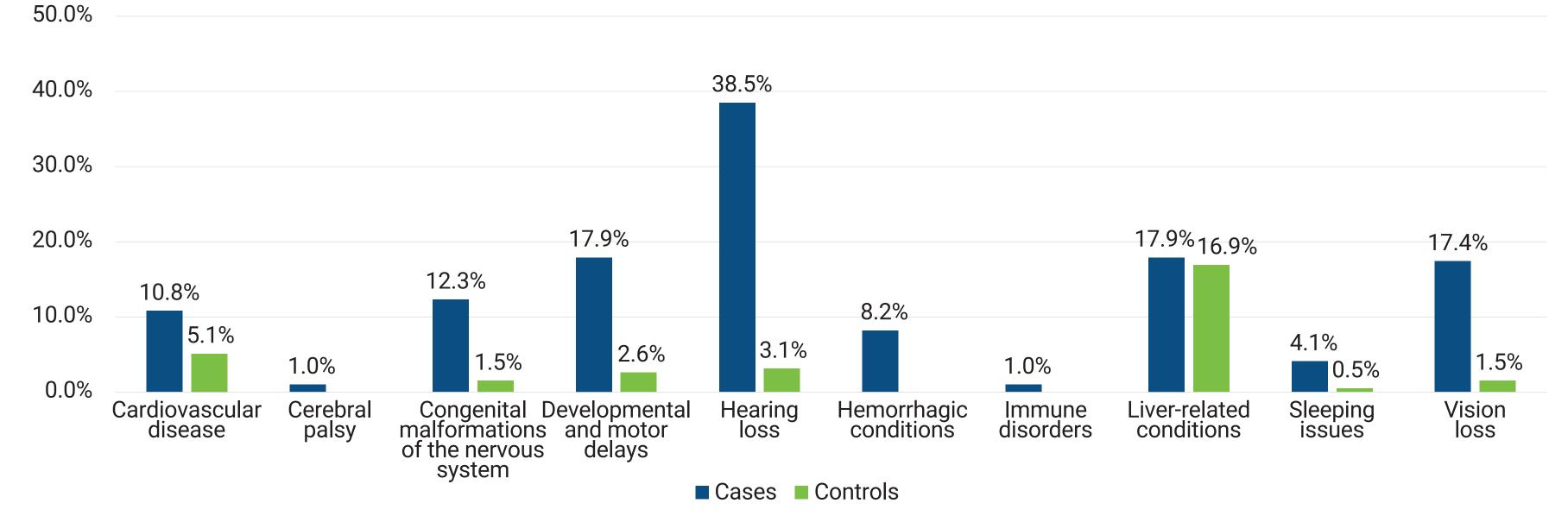
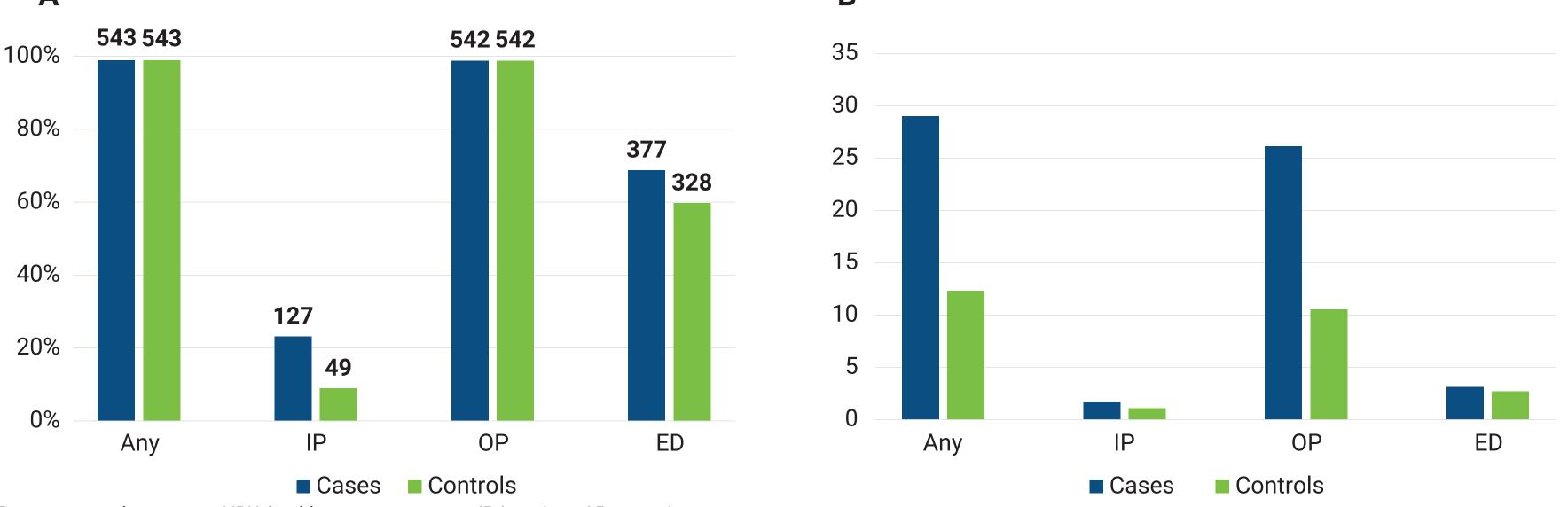


Figure 3. Number of Medicaid-insured cases and controls with HRU visits during the one-year study period (A) and the mean number of visits among Medicaid-insured patients with each visit type during the oneyear study period (B).



ED, emergency department: HRU, healthcare resource use: IP inpatient: OP outpatient Note: Lab/imaging visits were a subset of outpatient visits. During the one-year study period, 443 (80.7%) cases experienced a mean number of 5.5 lab/imaging visits, and 310 (56.5%) control patients experienced an average of 2.3 lab/imaging visits.

Table 3. All-cause healthcare costs among Medicaid-insured patients during the 1-year study period.

	Year 1		
All-cause costs ^{1,2}	Cases N = 549	Controls N = 549	P-value
Medical costs Mean ± SD Median [IQR]	\$13,212 ± \$45,789 \$2,800 [\$1,007 - \$7,525]	\$3,464 ± \$21,677 \$1,215 [\$572 - \$2,056]	<.0001
Inpatient costs Mean ± SD Median [IQR]	\$32,440 ± \$75,974 \$8,797 [\$1,973 - \$24,902]	\$20,350 ± \$68,465 \$4,202 [\$1,981 - \$9,189]	0.333
Outpatient costs Mean ± SD Median [IQR]	\$4,765 ± \$11,944 \$1,842 [\$775 - \$4,453]	\$1,259 ± \$2,336 \$930 [\$367 - \$1,459]	<.0001
Lab/imaging costs Mean ± SD Median [IQR]	\$698 ± \$3,566 \$172 [\$21 - \$517]	\$144 ± \$309 \$30 [\$3 - \$165]	0.001
ED costs Mean ± SD Median [IQR]	\$864 ± \$1,714 \$369 [\$121 - \$985]	\$541 ± \$699 \$276 [\$108 - \$697]	<.001
Pharmacy costs Mean ± SD Median [IQR]	\$2,353 ± \$4,809 \$262 [\$51 - \$2,312]	\$360 ± \$2,147 \$54 [\$15 - \$146]	<.0001

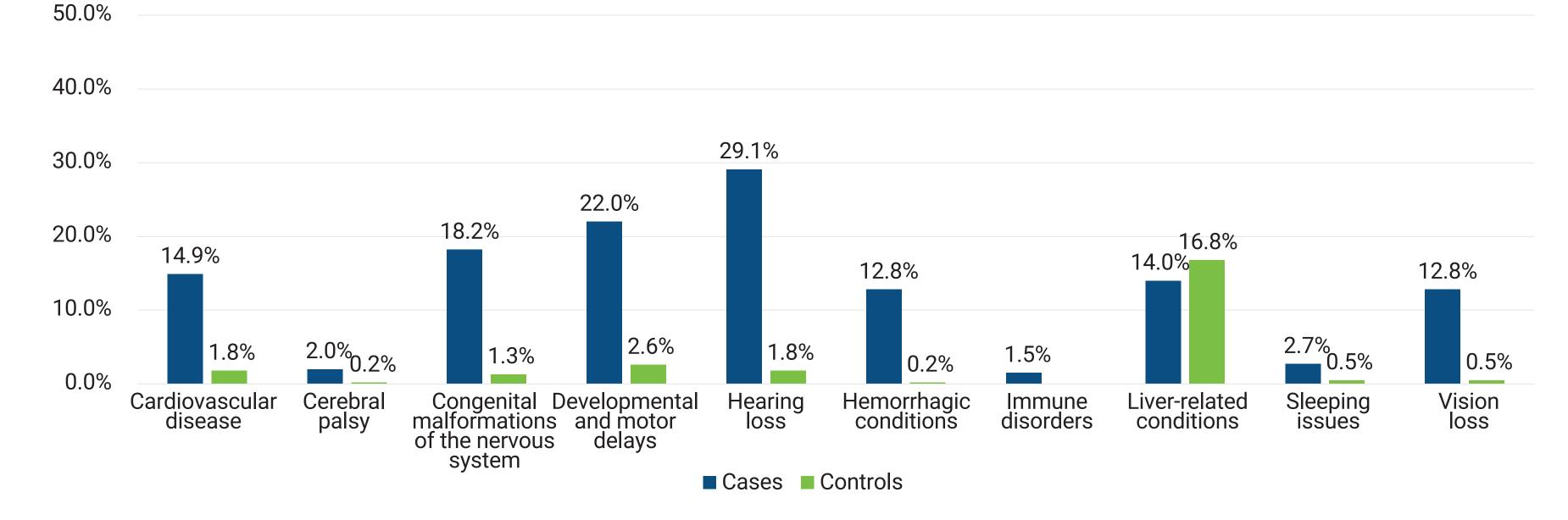
[1] Costs were summarized only among patients with that type of HRU during the study period.

[2] Costs were measured from the payer perspective and adjusted to 2021 USD (\$).

Among the 75 commercially-insured and 160 Medicaid-insured cCMV cases with hearing loss, 62.7% and 64.4% had a diagnosis of SNHL, respectively; other hearing loss was "unspecified".

- Among the commercially- and Medicaid-insured patients with cardiovascular disease during the study period, the majority of diagnoses were or chronic pulmonary disease and tachycardia.
- Liver related conditions were common among cases and controls in both payer populations, driven by high rates of pediatric jaundice.

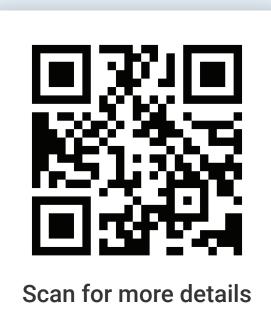
Figure 5. Commonly-observed sequelae among Medicaid-insured patients during the 1-year study period



Diagnoses and procedures were identified via codes used for administrative billing purposes and may be underestimated due to coding incompleteness or inaccuracies.

- CMV is a largely asymptomatic disease for which individuals are not always screened. This study does not account for undiagnosed cCMV and CMV.
- Potentially relevant clinical information such as laboratory results, clinical markers of disease severity or pathology, or symptoms of interest without associated claims codes cannot be assessed in this database.
- These results were limited to patients with commercial or Medicaid coverage in the US, and thus findings may not be generalizable to other patient populations.

- cCMV patients have substantial HRU and costs during the first year following cCMV diagnosis.
- While the majority of patients did not require hospitalization during the one-year study period, inpatient care contributed substantially to the overall cost burden.
- The largest economic burden was experienced in the first 0–6 months following cCMV diagnosis; however, all cCMV patients continued to have significant HRU and cost burden through the one-year study period.
- cCMV patients experienced higher rates of common sequelae during the first year following diagnosis compared to non-cCMV controls.
- Together, the variety of complications and the wide distribution of costs experienced by cCMV patients illustrate the clinical complexity of the disease.
- Future studies should evaluate longer-term costs beyond the first year as well as the reasons underlying the high economic burden among cCMV patients.



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