

Economic Burden of Diagnosed Congenital Cytomegalovirus in the United States and Japan

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BACKGROUND

- Congenital cytomegalovirus (cCMV) is the leading infectious cause of birth defects and neurological disabilities in high-income countries^{1,2}
 - Approximately 20-25% of infants born with cCMV develop symptoms or long-term complications such as hearing loss, developmental issues, and microcephaly^{1,4,7}
- Despite the risk of serious health complications, cCMV is difficult to diagnose because only 10-15% of infants with cCMV display symptoms at birth^{1,8,9}
- There are few recent studies on the economic burden of cCMV in the USA or Japan¹⁰⁻¹⁴

OBJECTIVES

- To assess healthcare resource utilization (HCRU) and cost burden among populations of infants diagnosed with cCMV in the USA and Japan using insurance claims data

METHODS

Data Sources and Cohort Selection

- This retrospective study utilized de-identified Merative MarketScan Commercial Claims and Encounters and Multi-State Medicaid data (2010-2019) and Japan Medical Data Center (JMDC) data (2011-2020)
 - US patients were included in either the commercially- or Medicaid-insured population
 - The JMDC database consisted of medical and pharmacy claims for beneficiaries and their dependents of the Kenpo health insurance system who were employed by middle- to large-size companies in Japan
- Separately by payer population, 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.x) within 1 month of birth (USA) or on a claim during the birth month or the first calendar month following the birth month (Japan)
- Patients were included in the control cohort ("controls") if they had no diagnosis of cCMV or CMV at any point during follow-up
- 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/CMV for cases; for controls, the index date was selected at random from all medical claims within 1 month of birth (USA) or from all medical claims during the birth month or following month (Japan)
- cCMV cases were matched 1:1 to controls on demographic characteristics, health insurance type (US only), birth year, and index year
- Patients were followed for 1 year post-index date (the "study period")

Study Outcomes

- All-cause HCRU and costs were assessed during the study period
 - HCRU categories assessed in the USA included all medical visits, inpatient (IP) admissions, emergency department (ED) visits, outpatient (OP) visits, lab/imaging visits (as a subset of OP), and pharmacy costs
 - For the USA, birth admissions were defined as the IP admission during which the patient was born and were described separately
 - HCRU categories assessed in Japan included: all medical visits, IP/Diagnosis Procedure Combination (DPC) admissions, OP visits, lab/imaging visits (as a subset of OP), and pharmacy costs
 - Costs were reported in 2021 USD (\$) and 2020 JPY (¥)
 - For each HCRU category, values were reported as the average total number of visits and average total costs per patient among patients with ≥1 visit of that type during the study period
- Comparisons between the matched case and control cohorts were conducted using Wilcoxon rank sum tests for continuous variables and chi-square tests for categorical variables

RESULTS

Patient Characteristics

- This analysis included 195 commercially-insured and 549 Medicaid-insured matched pairs from the USA and 152 matched pairs from Japan
 - Patient characteristics for each population are shown in **Table 1**

Table 1. Patient Characteristics at the Index Date Among Matched cCMV and Control Cohorts by Population

Characteristic	cCMV cohort / control cohort		
	US commercially-insured population (N = 195 matched pairs)	US Medicaid-insured population (N = 549 matched pairs)	Japanese population (N = 152 matched pairs)
Age (months), mean ± SD	0.3 ± 0.3 / 0.3 ± 0.3	0.2 ± 0.3 / 0.2 ± 0.3	0.3 ± 0.4 / 0.6 ± 0.5
Male, n (%)	96 (49.2) / 96 (49.2)	304 (55.4) / 304 (55.4)	77 (50.7) / 77 (50.7)
Insurance type (US only), n (%)			
HMO	29 (14.9) / 29 (14.9)	386 (70.3) / 386 (70.3)	-
POS	23 (11.8) / 23 (11.8)	1 (0.2) / 1 (0.2)	-
Non-HMO/POS	143 (73.3) / 143 (73.3)	162 (29.5) / 162 (29.5)	-
Facility setting (Japan only), n (%)			
Clinic	-	-	43 (28.3) / 63 (41.4)
University hospital	-	-	45 (29.6) / 5 (3.3)
Public hospital	-	-	26 (17.1) / 19 (12.5)
Other hospital	-	-	27 (17.8) / 49 (32.2)
Multiple settings	-	-	11 (7.2) / 16 (10.5)
First cCMV/CMV diagnosis, n (%)			
cCMV	130 (66.7) / 0 (0.0)	414 (75.4) / 0 (0.0)	108 (71.1) / 0 (0.0)
CMV	60 (30.8) / 0 (0.0)	123 (22.4) / 0 (0.0)	44 (28.9) / 0 (0.0)
Both cCMV and CMV	5 (2.6) / 0 (0.0)	12 (2.2) / 0 (0.0)	0 (0.0) / 0 (0.0)

cCMV, congenital cytomegalovirus; CMV, cytomegalovirus; HMO, health maintenance organization; POS, point of service; SD, standard deviation.

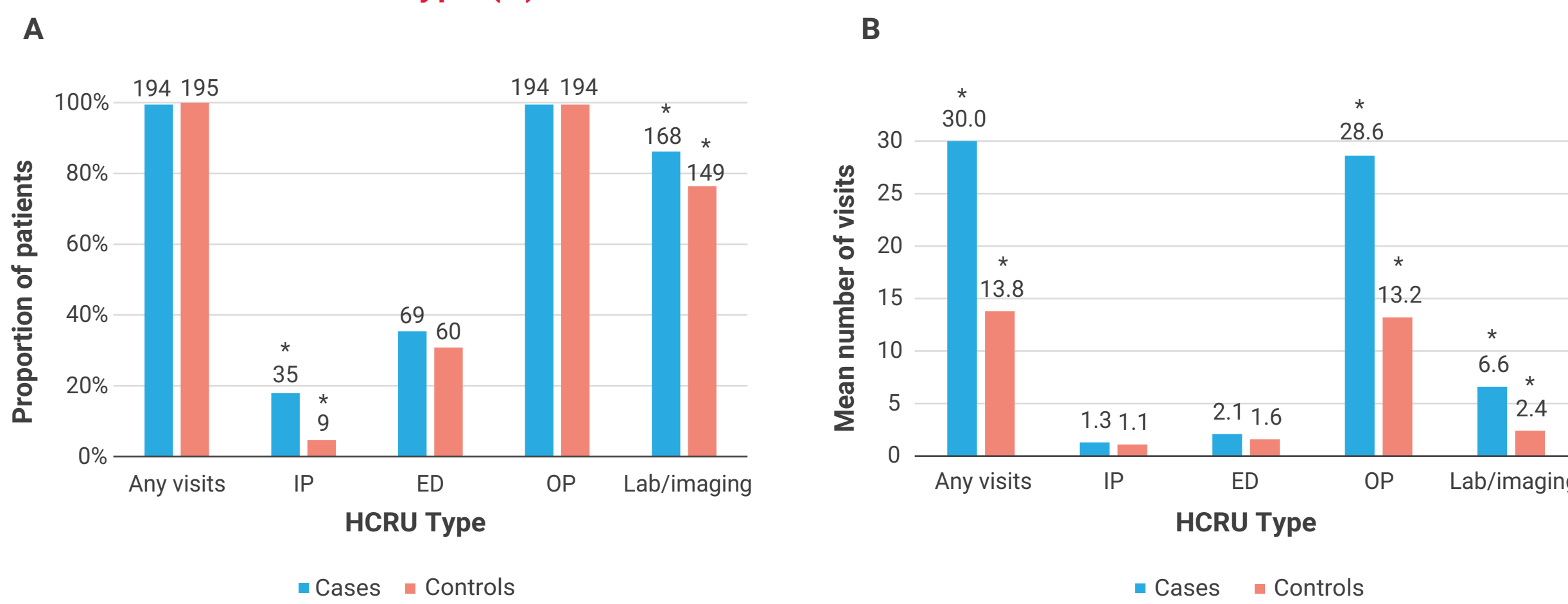
Note: Cases were matched 1:1 without replacement to controls based on demographic characteristics, health insurance type (US only), birth year, and index year.

RESULTS (continued)

All-Cause HCRU (USA)

- cCMV cases were significantly more likely than controls to have an IP admission and the mean number of total medical visits was significantly higher among commercially-insured cCMV cases vs controls (**Figure 1**), as well as among Medicaid-insured cCMV cases vs controls (**Figure 2**)
 - 84.1% of commercially-insured cases and 81.5% of controls had a birth admission captured in their medical claims, with the mean birth admission length of stay significantly longer for cases vs controls (23.7 ± 50.3 days vs 5.1 ± 10.0 days; P<0.0001)
 - 95.6% of Medicaid-insured cases and 94.4% of controls had a birth admission captured in their medical claims, with the mean birth admission length of stay significantly longer for cases vs controls (24.0 ± 37.5 days vs 5.2 ± 9.4 days; P<0.0001)

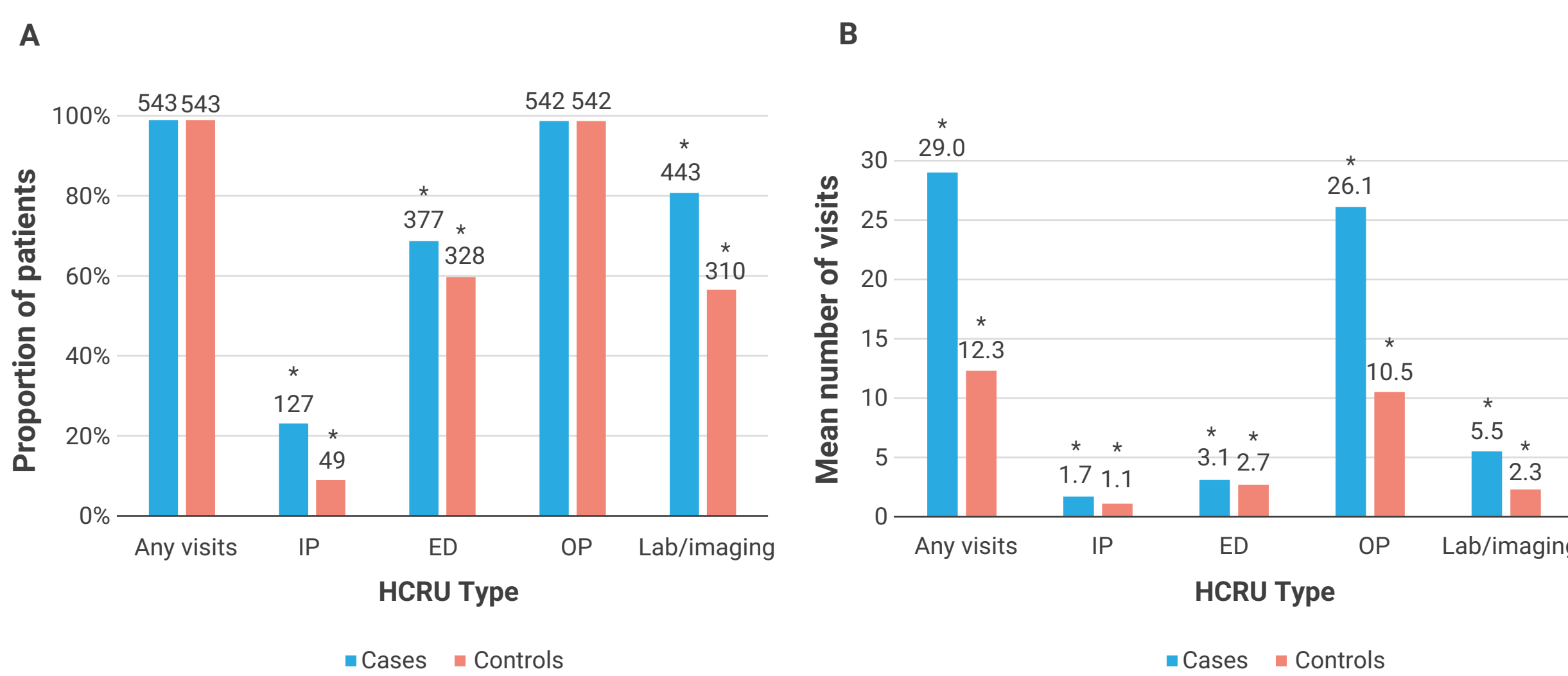
Figure 1. Number and Proportion of US Commercially-Insured cCMV Cases and Controls With HCRU During the 1-Year Study Period (A) and the Mean Number of Medical Visits Among Infants With Each Visit Type (B)



ED, emergency department; HCRU, healthcare resource utilization; IP, inpatient; OP, outpatient.

*denotes a P-value of <0.05; number of medical visits were summarized only among infants with at least 1 visit of that type during the study period.

Figure 2. Number and Proportion of US Medicaid-Insured cCMV Cases and Controls With HCRU During the 1-Year Study Period (A) and the Mean Number of Medical Visits Among Infants With Each Visit Type (B)



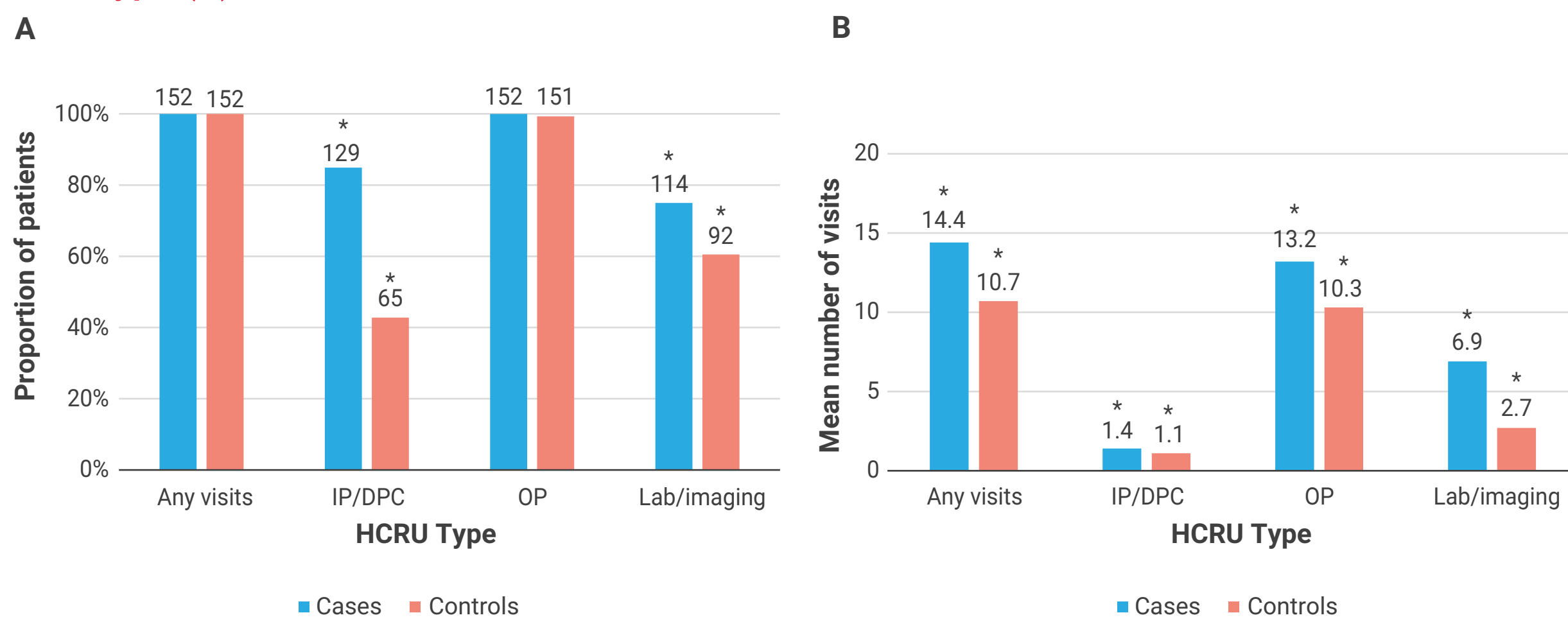
ED, emergency department; HCRU, healthcare resource utilization; IP, inpatient; OP, outpatient.

*denotes a P-value of <0.05; numbers of medical visits were summarized only among infants with at least 1 visit of that type during the study period.

All-Cause HCRU (Japan)

- cCMV cases were significantly more likely than controls to have an IP/DPC admission, and the mean number of total medical visits was significantly higher among cCMV cases vs controls (**Figure 3**)
 - The mean number of IP/DPC admissions was highest in the first 3 months after the index date for infants both with and without cCMV

Figure 3. Number and Proportion of Japanese cCMV Cases and Controls With HCRU During the 1-Year Study Period (A) and the Mean Number of Medical Visits Among Infants With Each Visit Type (B)



DPC, Diagnosis Procedure Combination; HCRU, healthcare resource utilization; IP, inpatient; OP, outpatient.

*denotes a P-value of <0.05; number of medical visits were summarized only among infants with at least 1 visit of that type during the study period.

All-Cause Costs (USA)

- Mean all-cause healthcare costs were significantly higher among commercially-insured cCMV cases vs controls (**Table 2**), as well as among Medicaid-insured cCMV cases vs controls (**Table 3**)
 - These differences were seen for birth admission costs, total post-birth medical costs, and pharmacy costs

Table 2. All-Cause Healthcare Costs Among US Commercially-Insured Infants During the 1-Year Study Period

Category	cCMV cohort (N = 195)	Control cohort (N = 195)	P-value
Birth admission costs			
Mean ± SD	\$149,192 ± 612,278	\$17,996 ± 86,130	<0.0001
Median [IQR]	\$19,002 [2408-89,044]	\$2669 [1642-4091]	
Post-birth medical costs			
Mean ± SD	\$38,742 ± 161,537	\$5519 ± 6813	<0.0001
Median [IQR]	\$9075 [3902-22,172]	\$3310 [2554-5334]	
IP			
Mean ± SD	\$121,981 ± 351,560	\$12,921 ± 10,357	0.099
Median [IQR]	\$21,036 [9595-60,106]	\$9858 [7679-17,263]	
ED			
Mean ± SD	\$1944 ± 3039	\$1708 ± 3749	0.070
Median [IQR]	\$1081 [319-2449]	\$564 [142-1435]	
OP			
Mean ± SD	\$15,451 ± 31,052	\$4358 ± 4875	<0.0001
Median [IQR]	\$6615 [3318-13,255]	\$3094 [2488-4371]	
Lab/imaging			
Mean ± SD	\$1662 ± 2927	\$302 ± 883	<0.0001
Median [IQR]	\$548 [92-2356]	\$32 [11-203]	
Pharmacy costs			
Mean ± SD	\$3019 ± 7862	\$330 ± 2494	<0.0001
Median [IQR]	\$283 [30-3053]	\$23 [0-107]	

cCMV, congenital cytomegalovirus; ED, emergency department; HCRU, healthcare resource utilization; IP, inpatient; IQR, interquartile range; OP, outpatient; SD, standard deviation.

Note: Costs were summarized only among infants with that type of HCRU during the study period and adjusted to 2021 USD (\$).

Table 3. All-Cause Healthcare Costs Among US Medicaid-Insured Infants During the 1-Year Study Period

Category	cCMV cohort (N = 549)	Control cohort (N = 549)	P-value
Birth admission costs			
Mean ± SD	\$49,885 ± 138,887	\$5052 ± 31,465	<0.0001
Median [IQR]	\$9874 [1484-31,331]	\$1540 [908-2324]	
Post-birth medical costs			
Mean ± SD	\$13,212 ± 45,789	\$3464 ± 21,677	<0.0001
Median [IQR]	\$2800 [1007-7525]	\$1215 [572-2056]	
IP			
Mean ± SD	\$32,440 ± 75,974	\$20,350 ± 68,465	0.009
Median [IQR]	\$8797 [1973-24,902]	\$4202 [1981-9189]	
ED			
Mean ± SD	\$864 ± 1714	\$541 ± 699	0.038
Median [IQR]	\$369 [121-985]	\$276 [108-697]	
OP			
Mean ± SD	\$4765 ± 11,944	\$1259 ± 2336	<0.0001
Median [IQR]	\$1842 [775-4453]	\$930 [367-1459]	
Lab/imaging			
Mean ± SD	\$698 ± 3566	\$144 ± 309	<0.0001
Median [IQR]	\$172 [21-517]	\$30 [3-165]	
Pharmacy costs			
Mean ± SD	\$2353 ± 4809	\$360 ± 2147	<0.0001
Median [IQR]	\$262 [51-2312]	\$54 [15-146]	

cCMV, congenital cytomegalovirus; ED, emergency department; HCRU, healthcare resource utilization; IP, inpatient; IQR, interquartile range; OP, outpatient; SD, standard deviation.

Note: Costs were summarized only among infants with that type of HCRU during the study period and were adjusted to 2021 USD (\$).

All-Cause Costs (Japan)

- Mean all-cause medical costs were significantly higher among cCMV cases vs controls (**Table 4**)
 - The greatest contributor was costs associated with IP/DPC admissions; mean pharmacy costs did not differ between infants with and without cCMV

Table 4. All-Cause Healthcare Costs Among Japanese Infants During the 1-Year Study Period

Category	cCMV cohort (N = 152)	Control cohort (N = 152)	P-value
Medical costs			
Mean ± SD	¥1,652,324 ± 3,406,084	¥274,652 ± 710,444	<0.0001
Median [IQR]	¥275,256 [135,346-1,548,964]	¥98,906 [53,868-211,061]	
IP/DPC			
Mean ± SD	¥1,617,178 ± 3,390,720	¥386,972 ± 882,965	0.019
Median [IQR]	¥247,584 [53,473-1,455,737]	¥134,492 [40,479-315,456]	
OP			
Mean ± SD	¥279,850 ± 422,999	¥109,893 ± 189,398	<0.0001
Median [IQR]	¥129,218 [63,126-254,746]	¥74,588 [41,550-114,387]	
Lab/imaging			
Mean ± SD	¥42,348 ± 40,421	¥11,347 ± 16,006	<0.0001
Median [IQR]	¥36,537 [9942-59,055]	¥5613 [2418-13,905]	
Pharmacy costs			
Mean ± SD	¥27,991 ± 37,041	¥25,477 ± 27,576	0.744
Median [IQR]	¥17,407 [7549-30,483]	¥18,359 [7110-37,310]	

cCMV, congenital cytomegalovirus; DPC, Diagnosis Procedure Combination; HCRU, healthcare resource utilization; IP, inpatient; IQR, interquartile range; OP, outpatient; SD, standard deviation.

Note: Costs were summarized only among infants with that type of HCRU during the study period and adjusted to 2020 JPY (¥).

CONCLUSIONS

- In both the USA and Japan, infants diagnosed with cCMV had substantial resource burden during their first year post-diagnosis, with 6-8 times greater incremental medical costs versus non-CMV controls
 - Inpatient care (including birth admissions) contributed substantially to the overall cost burden
- There are challenges with fully assessing the HCRU and economic burden of cCMV since universal screening for cCMV is not routinely conducted in the USA or Japan; thus, the burden of undiagnosed cCMV is not captured in this insurance claims-based analysis
 - Some of these undiagnosed cCMV cases are likely to be misclassified as non-cCMV controls; this misclassification bias may result in a conservative estimate of the cCMV burden relative to controls
- Future studies should evaluate the longer-term economic burden of diagnosed cCMV, as well as in additional countries where data are available

ADDITIONAL INFORMATION

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For additional information, please contact Philip Buck (Philip.Buck@modernatx.com).



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Disclosures

PB, SB, and JD-D are employees of Moderna, Inc., and hold stock/stock options in the company. AA, JRM, DG, KS, NK, and UD are full-time employees of Analysis Group, Inc., which received support from Moderna, Inc., for participation in this research.

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