

Direct Healthcare Costs Associated With Primary Symptomatic Cytomegalovirus in the United States

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BACKGROUND

- Cytomegalovirus (CMV) is a common herpes virus that affects at least half of adults globally.¹ In the United States, nearly 1 in 3 children is already infected with CMV by age 5, and over half of adults have been infected with CMV by age 40²
- Most healthy people who acquire a primary CMV infection have no or minor symptoms, such as fever and fatigue. Occasionally, however, primary CMV infection can cause mononucleosis or hepatitis²
 - Furthermore, individuals with weakened immune systems who become infected with CMV may also develop serious symptoms affecting the eyes, lungs, liver, esophagus, stomach, and intestines²
- To our knowledge, there are no published data on healthcare resource utilization (HCRU) or costs associated with symptomatic primary CMV

OBJECTIVE

- To examine the incremental HCRU and direct healthcare costs attributable to primary symptomatic (diagnosed) CMV relative to matched controls among commercially- and Medicaid-insured individuals in the United States using insurance claims data

METHODS

Study Design and Data

- This retrospective study utilized insurance claims data from the Merative MarketScan® Commercial Claims and Encounters (CCAЕ) and the Multi-State Medicaid Database during a pre–COVID-19 pandemic period (June 30, 2017, to February 29, 2020)
- The CMV cohort included individuals aged 9-50 years with ≥1 primary or ≥2 secondary diagnoses for CMV disease (ICD-10: B25.x), cytomegaloviral mononucleosis (ICD-10: B27.1x), or congenital CMV (cCMV, ICD-10: P35.1)
- CMV cases were matched 1:1 to controls (no CMV diagnosis at any point) on index date age, sex, geographic region of residence (commercially-insured individuals only), healthcare plan type, index year, race (Medicaid-insured individuals only), as well as on Quan-Charlson Comorbidity Index (QCCI) score and immunocompromised (IC) status assessed during the 6-month baseline period
 - The index date for the cases was defined as the first observed diagnosis of CMV in the data, and for the controls as the date of a HCRU visit which is ±7 days within the index date of the cases
- Individuals in the CMV and the matched control cohorts were excluded from the study if they had ≥1 diagnosis or procedure code for solid organ, stem cell, or blood transplant at any point during the study period or missing demographics on the index date (sex, healthcare plan type, race [Medicaid-insured individuals only], or geographic region [commercially-insured individuals only])
- All individuals were required to have had continuous healthcare plan enrollment for ≥6 months pre-index (baseline) and ≥6 months post-index (follow-up)

Study Outcomes and Analyses

- All-cause HCRU and direct healthcare costs (in 2022 USD) were assessed during the 6-month follow-up period (including 3-month time intervals)
 - The HCRU categories included: all visits, inpatient (IP) admissions, emergency department (ED) visits, and outpatient (OP) visits
 - Pharmacy costs were also assessed
- For each type of visit, values were reported as the mean and median total number of visits and the mean and median non-zero costs per individual among those with ≥1 visit during the follow-up period
- Categorical variables were compared using McNemar's tests; costs and number of HCRU visits were compared using Kruskal-Wallis tests

RESULTS

Patient Characteristics

- 845 commercially-insured and 295 Medicaid-insured matched pairs were included (**Supplementary Figure 1**)
- Among commercially-insured CMV cases and non-CMV controls, the mean (SD) age was 31 (11) years, 62% were female, and 13% were immunocompromised. Among Medicaid-insured CMV cases and non-CMV controls, the mean (SD) age was 23 (11) years, 67% were female, and 14% were immunocompromised (**Table 1**)
- Commercially-insured CMV cases were on average almost 8 years older and had fewer comorbidities compared with their Medicaid-insured counterparts. The mean (SD) QCCI score was 0.65 (1.67) for commercially-insured CMV cases and 1.00 (2.04) for Medicaid-insured CMV cases

All-Cause HCRU

- Over the 6-month follow-up period, commercially-insured CMV cases and non-CMV controls experienced a mean (SD) of 12.3 (11.7) and 8.2 (10.0) medical visits, respectively ($P<0.001$) (**Figure 1, Supplementary Table 1**). Medicaid-insured CMV cases and controls experienced a mean (SD) of 28.7 (42.0) and 12.1 (14.9) medical visits, respectively ($P<0.001$) (**Figure 2, Supplementary Table 2**)
- Commercially-insured CMV cases had a mean (SD) of 1.3 (0.8) IP admissions with a mean (SD) length of stay (LOS) of 13.0 (22.2) days compared with 1.1 (0.4) IP admissions with a LOS of 6.8 (13.4) days for the controls ($P<0.01$) (**Figure 1, Supplementary Table 1**). The mean (SD) number of OP and ED visits were 11.7 (11.1) and 1.8 (1.3) for the CMV cases, and 8.1 (9.9) and 1.5 (1.0) for the controls, respectively, both significantly higher for the cases (all $P<0.01$)
- Medicaid-insured CMV cases had a mean (SD) of 1.4 (1.0) IP admissions with a mean (SD) LOS of 12.4 (15.0) compared with 1.3 (0.9) IP admissions with a LOS of 6.1 (10.4) for the controls ($P=0.029$) (**Figure 2, Supplementary Table 2**). The mean (SD) number of OP visits for the CMV cases and controls were 27.2 (41.9) and 11.4 (14.8), respectively ($P<0.001$). The mean (SD) number of ED visits were 2.8 (3.1) and 2.1 (1.6), respectively ($P=0.262$)
- Medicaid-insured CMV cases had generally a higher number of HCRU visits (primarily driven by a higher number of OP visits) during the 6-month follow-up period compared with commercially-insured CMV cases: the mean (SD) number of total visits was 28.7 (42.0) vs 12.3 (11.7), respectively

All-Cause Costs

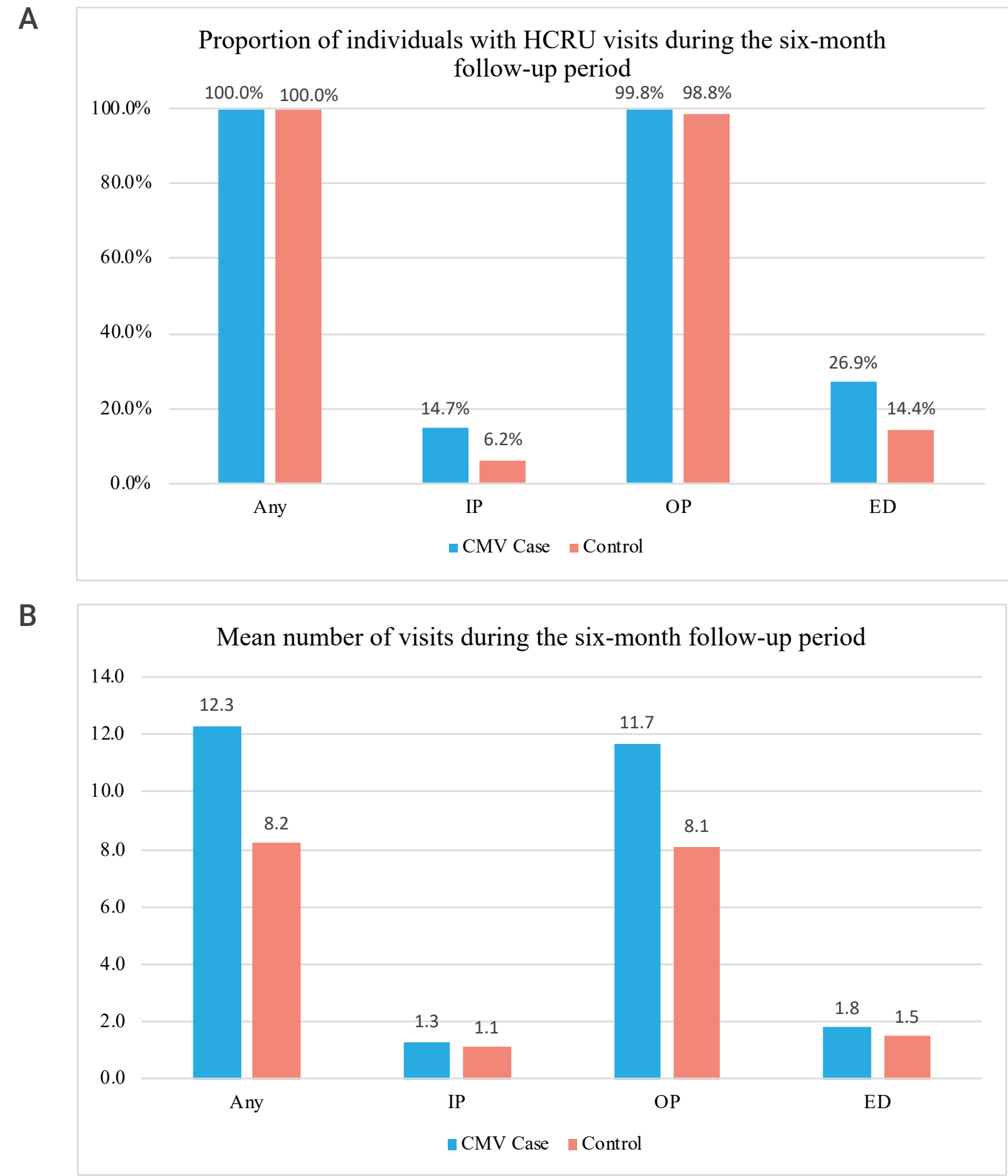
- Among the commercially-insured population, median medical costs during the 6-month follow-up period were \$3223 (interquartile range [IQR]: \$1030-\$15,466) for the CMV cases and \$1098 [\$392-\$4509] for the controls (**Table 2**). Excess medical costs due to CMV were estimated at \$2125 ($P<0.001$)
 - More than half of the median medical costs for the cases and controls occurred in the first 3 months post-index
 - While only 14.7% of CMV cases were hospitalized and 26.9% had ED visits during the 6-month follow-up (**Figure 1**), the associated costs were substantial: median [IQR] of \$20,778 [\$14,026-\$54,027] for IP costs and \$6934 [\$2054-\$25,237] for ED costs
- Median pharmacy costs were more than double for the commercially-insured CMV cases compared with the controls: \$266 [\$57-\$1752] vs \$107 [\$31-\$480], respectively ($P<0.001$)
- Among the Medicaid-insured population, median [IQR] medical costs during the 6-month follow-up period were \$2264 [\$621-\$14,127] for the CMV cases and \$851 [\$299-\$3023] for the controls (**Table 2**). Excess medical costs due to CMV were estimated at \$1413 ($P<0.001$)
 - Over 60% of the median medical costs for the cases and controls occurred in the first 3 months post-index
 - Among the CMV cases that were hospitalized (18.3%) or had ED visits (50.5%) during the 6-month follow-up (**Figure 2**), the median [IQR] was \$9990 [\$3779-\$36,517] for IP costs and \$2200 [\$579-\$8358] for ED costs
 - Median [IQR] pharmacy costs for the Medicaid-insured CMV cases were more than 5 times as much as those of controls: \$806 [\$100-\$4900] vs \$150 [\$17-\$544], respectively ($P<0.001$)
 - Medicaid-insured CMV cases had lower total costs (medical + pharmacy) during the 6-month follow-up period compared with commercially-insured CMV cases: the median [IQR] was \$3500 [\$770-\$21,060] vs \$4689 [\$1378-\$20,067], respectively (**Supplementary Tables 1 & 2**)

Table 1. Patient Characteristics for the Commercially- and Medicaid-Insured Populations

	Commercially insured population*		Medicaid-insured population*	
	CMV cases N = 845	Matched controls N = 845	CMV cases N = 295	Matched controls N = 295
Age on the index date, mean (SD)	30.94 (10.72)	30.94 (10.70)	23.32 (10.81)	23.36 (10.85)
Female, n (%)	527 (62.4)	527 (62.4)	198 (67.1)	198 (67.1)
Region, n (%)				
Northeast	174 (20.6)	174 (20.6)	N/A	N/A
North Central	157 (18.6)	157 (18.6)	N/A	N/A
South	380 (45.0)	380 (45.0)	N/A	N/A
West	134 (15.9)	134 (15.9)	N/A	N/A
Race, n (%)				
White	N/A	N/A	183 (62.0)	183 (62.0)
Black	N/A	N/A	97 (32.9)	97 (32.9)
Hispanic	N/A	N/A	6 (2.0%)	6 (2.0)
Other	N/A	N/A	9 (3.1%)	9 (3.1)
Insurance type, n (%)				
HMO	110 (13.0)	110 (13.0)	193 (65.4)	193 (65.4)
POS	72 (8.5)	72 (8.5)	3 (1.0)	3 (1.0)
Other ^a	663 (78.5)	663 (78.5)	99 (33.6)	99 (33.6)
Index year, n (%)				
2017	2 (0.2)	2 (0.2)	1 (0.3)	1 (0.3)
2018	532 (63.0)	532 (63.0)	184 (62.4)	184 (62.4)
2019	311 (36.8)	311 (36.8)	110 (37.3)	110 (37.3)
Presence of IC conditions, n (%)	110 (13.0)	110 (13.0)	40 (13.6)	40 (13.6)
QCCI score, n (%)				
0	627 (74.2)	627 (74.2)	178 (60.3)	178 (60.3)
1	123 (14.6)	123 (14.6)	69 (23.4)	69 (23.4)
2	32 (3.8)	32 (3.8)	21 (7.1)	21 (7.1)
≥3	63 (7.5)	63 (7.5)	27 (9.2)	27 (9.2)
QCCI score, mean (SD)	0.65 (1.67)	0.65 (1.66)	1.00 (2.04)	0.87 (1.70)

CMV, cytomegalovirus; HMO, health maintenance organization; IC, immunocompromising; POS, point-of-service; QCCI, Quan-Charlson Comorbidity Index; SD, standard deviation.
^aP-value <0.05 for all patient characteristics for the CMV cases and matched controls, indicating there are no statistically significant differences between the 2 groups.
^bOther insurance types included comprehensive, preferred provider organization, exclusive provider organization, consumer-driven health plan, and high-deductible health plan.

Figure 1. All-Cause HCRU Among Commercially-Insured Individuals



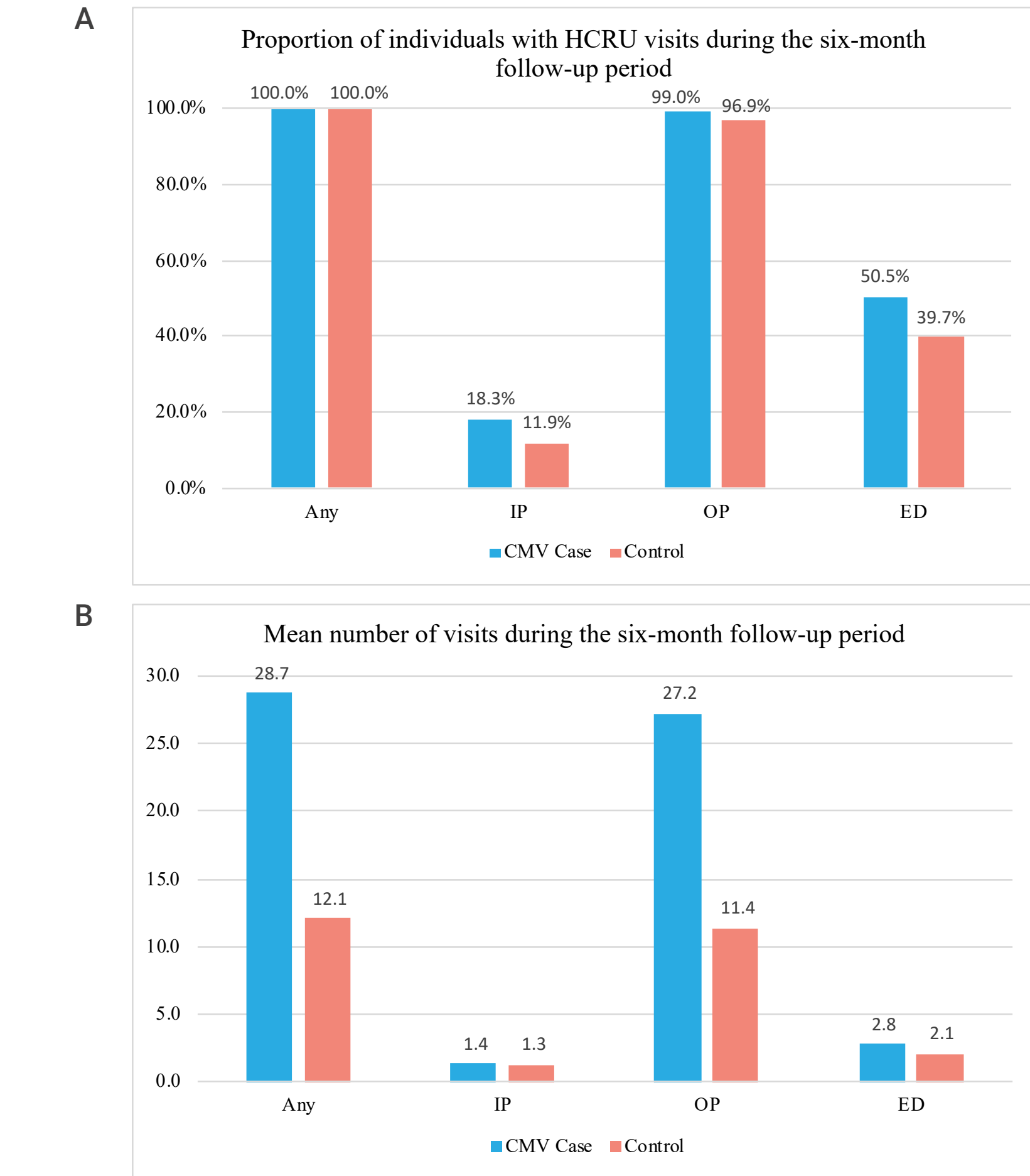
ED, emergency department; HCRU, healthcare resource utilization; IP, inpatient; OP, outpatient.

Table 2. All-Cause Costs for the Commercially- and Medicaid-Insured Populations During the 6-Month Follow-Up

	Commercially insured population			Medicaid-insured population		
	CMV cases N = 845	Matched controls N = 845	P-value	CMV cases N = 295	Matched controls N = 295	P-value
Medical costs						
Mean ± SD	\$23,995 ± \$82,516	\$7572 ± \$22,429		\$18,950 ± \$55,415	\$5149 ± \$25,057	
Median [IQR]	\$3223 [\$1030-\$15,466]	\$1098 [\$392-\$4509]	<0.001*	\$2264 [\$621-\$14,127]	\$851 [\$299-\$3023]	<0.001*
Inpatient costs						
Mean ± SD	\$70,973 ± \$148,694	\$26,100 ± \$31,768		\$51,665 ± \$106,524	\$29,303 ± \$76,842	
Median [IQR]	\$20,778 [\$14,026-\$54,027]	\$15,636 [\$12,758-\$29,204]	0.028*	\$9990 [\$3779-\$36,517]	\$4050 [\$1320-\$8,672]	0.150
Outpatient costs						
Mean ± SD	\$6087 ± \$13,025	\$5345 ± \$18,999		\$9925 ± \$22,028	\$2074 ± \$5306	
Median [IQR]	\$2023 [\$782-\$5710]	\$879 [\$340-\$2580]	<0.001*	\$1461 [\$536-\$6107]	\$572 [\$216-\$1821]	<0.001*
ED costs						
Mean ± SD	\$27,709 ± \$69,244	\$4685 ± \$6812		\$8871 ± \$19,816	\$2432 ± \$5768	
Median [IQR]	\$6934 [\$2054-\$25,237]	\$2300 [\$1199-\$4471]	<0.001*	\$2200 [\$579-\$8358]	\$590 [\$341-\$1630]	0.002*
Pharmacy costs						
Mean ± SD	\$4390 ± \$22,979	\$2135 ± \$7661		\$5838 ± \$11,409	\$1437 ± \$4974	
Median [IQR]	\$266 [\$57-\$1752]	\$107 [\$31-\$480]	<0.001*	\$806 [\$100-\$4900]	\$150 [\$17-\$544]	<0.001*

CMV, cytomegalovirus; ED, emergency department; IQR, interquartile range; SD, standard deviation.
*denotes a P-value of <0.05.

Figure 2. All-Cause HCRU Among Medicaid-Insured Individuals



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

CONCLUSIONS

- Commercially- and Medicaid-insured individuals diagnosed with primary CMV infection had significantly higher all-cause costs and HCRU during the 6 months post-diagnosis than non-CMV controls
- While most individuals did not require hospitalization during the 6-month follow-up, inpatient care contributed substantially to the overall cost burden
- CMV prevention such as a vaccine may have a positive impact on this healthcare burden

Limitations

- Diagnoses and procedures were identified via codes used for administrative billing purposes and may be subject to potential coding incompleteness or inaccuracies
- CMV is a largely asymptomatic disease for which individuals are not always screened. This study does not account for undiagnosed CMV. Furthermore, the claims databases used in the current study did not contain laboratory results confirming the diagnosis of CMV

ADDITIONAL INFORMATION

Please scan the QR code for a PDF copy of the poster and supplementary material. Copies of the poster and supplementary material obtained through the QR code are for personal use only and may not be reproduced without written permission of the authors.



For additional information, please contact Mihaela Georgieva (Mihaela.Georgieva@modernatx.com).

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Disclosures

MG, JW, TL, JDD, CK, and PB are employees of Moderna, Inc., and hold stock/stock options in the company. SH was an employee of Moderna, Inc., at the time of conducting this study.

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