

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

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SUPPLEMENTARY MATERIAL

Figure 1. Sample Selection

≥ 1 primary or ≥ 2 secondary diagnoses for CMV disease, CMV mononucleosis, or cCMV between June 30, 2017 to February 29, 2020 N (Commercial) = 5,564 N (Medicaid) = 3,500
≥ 6 months of continuous enrollment prior to the index date N (Commercial) = 2,693 N (Medicaid) = 974
Aged 9-50 years at index N (Commercial) = 1,623 N (Medicaid) = 615
No diagnoses of solid organ, stem cell or blood transplants at any point during the study period N (Commercial) = 1,111 N (Medicaid) = 420
No missing demographics* at index N (Commercial) = 1,081 N (Medicaid) = 379
≥ 6 months of continuous enrollment following the index date N (Commercial) = 870 N (Medicaid) = 319
Matched 1:1 to non-CMV controls on age, sex, region§, plan type, index year, race§, QCCI score, and IC status N (Commercial) = 845 N (Medicaid) = 295

CMV, cytomegalovirus; cCMV, congenital cytomegalovirus; QCCI, Quan-Charlson Comorbidity Index; IC, immunocompromised
*Demographics on the index date include sex, health plan indicator, race (Medicaid insured patients only), or geographic region (Commercially-insured patients only)
§ Region of residence is available for commercially-insured individuals only, while race is available for Medicaid-insured individuals only.

Supplementary Table 1. All-Cause HCRU and Costs – Commercially Insured Population

	Baseline			0-6 months follow-up			0-3 months follow-up			4-6 months follow-up						
	CMV cases N = 845	Matched controls N = 845	P-value	CMV cases N = 845	Matched controls N = 845	P-value	CMV cases N = 845	Matched controls N = 845	P-value	CMV cases N = 845	Matched controls N = 845	P-value				
All-cause HCRU ever during each time period																
Total visits, n (%)	830 (98.2)	658 (77.9)	<0.001	*	845 (100.0)	845 (100.0)	N/A	845 (100.0)	845 (100.0)	N/A	687 (81.3)	538 (63.7)	<0.001	*		
Inpatient admissions, n (%)	57 (6.7)	27 (3.2)	<0.001	*	124 (14.7)	52 (6.2)	<0.001	*	94 (11.1)	33 (3.9)	<0.001	*	40 (4.7)	20 (2.4)	0.013	*
Outpatient visits, n (%)	829 (98.1)	651 (77.0)	<0.001	*	843 (99.8)	835 (98.8)	0.043	*	842 (99.6)	832 (98.5)	0.024	*	684 (80.9)	535 (63.3)	<0.001	*
Lab/imaging visits, n (%)	797 (94.3)	524 (62.0)	<0.001	*	799 (94.6)	638 (75.5)	<0.001	*	767 (90.8)	560 (66.3)	<0.001	*	541 (64.0)	369 (43.7)	<0.001	*
ED visits, n (%)	263 (31.1)	115 (13.6)	<0.001	*	227 (26.9)	122 (14.4)	<0.001	*	184 (21.8)	88 (10.4)	<0.001	*	90 (10.7)	44 (5.2)	<0.001	*
Pharmacy claims, n (%)	736 (87.1)	539 (63.8)	<0.001	*	732 (86.6)	618 (73.1)	<0.001	*	668 (79.1)	563 (66.6)	<0.001	*	614 (72.7)	435 (51.5)	<0.001	*
All-cause HCRU																
Total visits																
Mean ± SD	10.5 ± 9.9	7.4 ± 10.0			12.3 ± 11.7	8.2 ± 10.0			7.2 ± 6.5	5.3 ± 6.3			6.3 ± 6.6	4.7 ± 5.7		
Median [IQR]	8.0 [4.0-14.0]	4.0 [2.0-8.0]	<0.001	*	8.0 [5.0-16.0]	5.0 [2.0-10.0]	<0.001	*	5.0 [3.0-9.0]	3.0 [1.0-6.0]	<0.001	*	4.0 [2.0-8.0]	3.0 [1.0-5.8]	<0.001	*
Inpatient admissions																
Mean ± SD	1.2 ± 0.5	1.2 ± 0.5			1.3 ± 0.8	1.1 ± 0.4			1.2 ± 0.6	1.0 ± 0.2			1.1 ± 0.5	1.2 ± 0.4		
Median [IQR]	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.925		1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.084		1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.053		1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.390	
Inpatient days																
Mean ± SD	6.6 ± 7.2	7.8 ± 8.9			13.0 ± 22.2	6.8 ± 13.4			13.5 ± 18.9	7.3 ± 15.7			8.3 ± 14.5	5.3 ± 5.3		
Median [IQR]	4.0 [3.0-7.0]	4.0 [3.0-8.0]	0.491		5.0 [3.0-11.0]	3.5 [3.0-5.3]	0.003	*	6.0 [3.0-13.5]	3.0 [3.0-4.0]	<0.001	*	4.0 [3.0-6.0]	4.0 [3.0-7.0]	0.844	
Outpatient visits																
Mean ± SD	9.8 ± 9.6	7.1 ± 9.7			11.7 ± 11.1	8.1 ± 9.9			6.7 ± 6.1	5.2 ± 6.2			6.1 ± 6.3	4.5 ± 5.6		
Median [IQR]	7.0 [4.0-13.0]	4.0 [2.0-8.0]	<0.001	*	8.0 [4.0-15.0]	5.0 [2.0-10.0]	<0.001	*	5.0 [3.0-9.0]	3.0 [1.0-6.0]	<0.001	*	4.0 [2.0-8.0]	3.0 [1.0-5.0]	<0.001	*
Lab/imaging visits																
Mean ± SD	4.9 ± 4.3	3.4 ± 4.4			5.6 ± 5.5	3.8 ± 5.2			3.6 ± 3.2	2.8 ± 3.6			3.2 ± 3.3	2.4 ± 2.9		
Median [IQR]	4.0 [2.0-6.0]	2.0 [1.0-4.0]	<0.001	*	4.0 [2.0-7.0]	2.0 [1.0-4.0]	<0.001	*	3.0 [1.0-5.0]	2.0 [1.0-3.0]	<0.001	*	2.0 [1.0-4.0]	1.0 [1.0-3.0]	<0.001	*
ED visits																
Mean ± SD	1.8 ± 1.3	1.7 ± 1.3			1.8 ± 1.3	1.5 ± 1.0			1.5 ± 1.1	1.4 ± 0.9			1.5 ± 1.0	1.3 ± 0.6		
Median [IQR]	1.0 [1.0-2.0]	1.0 [1.0-2.0]	0.141		1.0 [1.0-2.0]	1.0 [1.0-2.0]	0.006	*	1.0 [1.0-2.0]	1.0 [1.0-1.0]	0.341		1.0 [1.0-2.0]	1.0 [1.0-2.0]	0.387	
All-cause costs																
Total costs (medical + pharmacy)																
Mean ± SD	\$13,913 ± \$42,142	\$8431 ± \$24,589			\$27,745 ± \$87,455	\$9115 ± \$24,001			\$21,074 ± \$76,512	\$5745 ± \$15,882			\$7568 ± \$20,091	\$4604 ± \$13,083		
Median [IQR]	\$3944 [\$1205-\$12,688]	\$1081 [\$322-\$3864]	<0.001	*	\$4689 [\$1378-\$20,067]	\$1506 [\$532-\$6188]	<0.001	*	\$2354 [\$722-\$12,238]	\$858 [\$307-\$3248]	<0.001	*	\$1444 [\$409-\$5678]	\$608 [\$204-\$2648]	<0.001	*
Medical costs																
Mean ± SD	\$11,740 ± \$40,929	\$8027 ± \$24,903			\$23,995 ± \$82,516	\$7572 ± \$22,429			\$19,077 ± \$74,474	\$4979 ± \$15,350			\$6081 ± \$17,396	\$4099 ± \$13,015		
Median [IQR]	\$2937 [\$966-\$9263]	\$926 [\$304-\$3043]	<0.001	*	\$3223 [\$1030-\$15,466]	\$1098 [\$392-\$4509]	<0.001	*	\$1714 [\$533-\$8930]	\$618 [\$230-\$2337]	<0.001	*	\$1029 [\$371-\$3925]	\$558 [\$195-\$1896]	<0.001	*
Inpatient costs																
Mean ± SD	\$49,509 ± \$122,440	\$34,566 ± \$29,281			\$70,973 ± \$148,694	\$26,100 ± \$31,768			\$82,061 ± \$161,538	\$29,160 ± \$38,735			\$27,173 ± \$38,240	\$19,747 ± \$12,545		
Median [IQR]	\$19,575 [\$12,663-\$36,026]	\$21,589 [\$15,493-\$51,761]	0.464		\$20,778 [\$14,026-\$54,027]	\$15,636 [\$12,758-\$29,204]	0.028	*	\$26,149 [\$15,533-\$68,428]	\$16,503 [\$12,720-\$29,696]	0.016	*	\$16,990 [\$9773-\$24,942]	\$14,582 [\$12,369-\$23,725]	0.913	
Outpatient costs																
Mean ± SD	\$5428 ± \$13,053	\$4929 ± \$16,390			\$6087 ± \$13,025	\$5345 ± \$18,999			\$3362 ± \$6740	\$3474 ± \$11,706			\$3371 ± \$8521	\$2963 ± \$11,112		
Median [IQR]	\$1818 [\$781-\$4669]	\$733 [\$274-\$2188]	<0.001	*	\$2023 [\$782-\$5710]	\$879 [\$340-\$2580]	<0.001	*	\$1197 [\$406-\$3202]	\$521 [\$219-\$1684]	<0.001	*	\$933 [\$345-\$2744]	\$477 [\$177-\$1270]	<0.001	*
Lab/imaging visits																
Mean ± SD	\$2197 ± \$3790	\$1726 ± \$4964			\$2149 ± \$4257	\$1885 ± \$7903			\$1410 ± \$2806	\$1399 ± \$6387			\$1189 ± \$2841	\$1138 ± \$5291		
Median [IQR]	\$869 [\$252-\$2606]	\$291 [\$79-\$1239]	<0.001	*	\$821 [\$238-\$2146]	\$368 [\$104-\$1234]	<0.001	*	\$451 [\$119-\$1434]	\$281 [\$78-\$916]	<0.001	*	\$426 [\$109-\$1194]	\$202 [\$57-\$713]	<0.001	*
ED costs																
Mean ± SD	\$9233 ± \$16,462	\$9974 ± \$22,512			\$27,709 ± \$69,244	\$4685 ± \$6812			\$29,963 ± \$74,631	\$3953 ± \$6165			\$8632 ± \$18,539	\$5176 ± \$7112		
Median [IQR]	\$4474 [\$1793-\$9818]	\$2476 [\$1342-\$5966]	0.004	*	\$6934 [\$2054-\$25,237]	\$2300 [\$1199-\$4471]	<0.001	*	\$8770 [\$2189-\$25,709]	\$1997 [\$1096-\$3745]	<0.001	*	\$2514 [\$1525-\$7195]	\$2922 [\$1627-\$4439]	0.970	
Pharmacy costs																
Mean ± SD	\$2557 ± \$8211	\$1414 ± \$4975			\$4,390 ± \$22,979	\$2135 ± \$7661			\$2608 ± \$13,640	\$1175 ± \$3972			\$2396 ± \$11,100	\$1514 ± \$5000		
Median [IQR]	\$189 [\$51-\$1127]	\$74 [\$21-\$291]	<0.001	*	\$266 [\$57-\$1,752]	\$107 [\$31-\$480]	<0.001	*	\$154 [\$33-\$1010]	\$67 [\$18-\$254]	<0.001	*	\$132 [\$30-\$1021]	\$71 [\$22-\$389]	<0.001	*

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

Supplementary Table 2. All-Cause HCRU and Costs -- Medicaid-Insured Population

	Baseline			6 months follow-up			0-3 months follow-up			4-6 months follow-up						
	CMV cases N = 295	Matched controls N = 295	P-value	CMV cases N = 295	Matched controls N = 295	P-value	CMV cases N = 295	Matched controls N = 295	P-value	CMV Cases N = 295	Matched controls N = 295	P-value				
All-cause HCRU, ever during each time period																
Total visits, n (%)	285 (96.6)	245 (83.1)	<0.001	*	295 (100.0)	295 (100.0)	N/A		295 (100.0)	295 (100.0)	N/A		260 (88.1)	213 (72.2)	<0.001	*
Inpatient admissions, n (%)	31 (10.5)	13 (4.4)	0.006	*	54 (18.3)	35 (11.9)	0.026	*	43 (14.6)	21 (7.1)	0.006	*	19 (6.4)	15 (5.1)	0.584	
Outpatient visits, n (%)	283 (95.9)	236 (80.0)	<0.001	*	292 (99.0)	286 (96.9)	0.114		292 (99.0)	281 (95.3)	0.010	*	252 (85.4)	206 (69.8)	<0.001	*
Lab/imaging visits, n (%)	246 (83.4)	179 (60.7)	<0.001	*	268 (90.8)	228 (77.3)	<0.001	*	252 (85.4)	211 (71.5)	<0.001	*	180 (61.0)	134 (45.4)	<0.001	*
ED visits, n (%)	151 (51.2)	108 (36.6)	<0.001	*	149 (50.5)	117 (39.7)	0.006	*	118 (40.0)	92 (31.2)	0.021	*	78 (26.4)	54 (18.3)	0.019	*
Pharmacy claims, n (%)	259 (87.8)	192 (65.1)	<0.001	*	265 (89.8)	218 (73.9)	<0.001	*	244 (82.7)	197 (66.8)	<0.001	*	228 (77.3)	163 (55.3)	<0.001	*
All-cause HCRU																
Total visits																
Mean ± SD	26.7 ± 41.4	8.6 ± 9.1			28.7 ± 42.0	12.1 ± 14.9			15.2 ± 20.9	7.3 ± 8.4			15.2 ± 22.5	6.6 ± 9.1		
Median [IQR]	12.0 [6.0-21.0]	6.0 [2.0-12.0]	<0.001	*	13.0 [7.0-26.0]	7.0 [3.0-15.0]	<0.001	*	7.0 [4.0-14.0]	5.0 [2.0-9.0]	<0.001	*	6.0 [3.0-14.3]	4.0 [2.0-8.0]	<0.001	*
Inpatient admissions																
Mean ± SD	1.4 ± 0.9	1.2 ± 0.6			1.4 ± 1.0	1.3 ± 0.9			1.2 ± 0.6	1.3 ± 0.7			1.4 ± 0.6	1.2 ± 0.8		
Median [IQR]	1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.571		1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.273		1.0 [1.0-1.0]	1.0 [1.0-1.0]	0.760		1.0 [1.0-2.0]	1.0 [1.0-1.0]	0.110	
Inpatient days																
Mean ± SD	8.4 ± 12.0	9.9 ± 10.4			12.4 ± 15.0	6.1 ± 10.4			10.7 ± 13.5	5.0 ± 3.7			10.8 ± 10.0	7.3 ± 14.1		
Median [IQR]	5.0 [3.0-7.0]	5.0 [3.0-10.0]	0.585		6.0 [3.0-15.0]	4.0 [3.0-5.0]	0.029	*	6.0 [3.0-10.0]	4.0 [3.0-5.0]	0.137		8.0 [3.5-13.0]	3.0 [3.0-4.5]	0.052	
Outpatient visits																
Mean ± SD	25.1 ± 41.4	7.9 ± 8.8			27.2 ± 41.9	11.4 ± 14.8			14.4 ± 20.9	7.0 ± 8.4			14.9 ± 22.6	6.3 ± 9.0		
Median [IQR]	10.0 [5.0-18.0]	5.0 [2.0-10.0]	<0.001	*	11.0 [6.0-24.0]	6.0 [3.0-13.8]	<0.001	*	7.0 [4.0-13.0]	4.0 [2.0-8.0]	<0.001	*	6.0 [3.0-13.3]	4.0 [1.0-7.8]	<0.001	*
Lab/imaging visits																
Mean ± SD	5.3 ± 4.6	4.3 ± 4.0			5.7 ± 5.6	4.6 ± 4.6			3.7 ± 3.3	3.3 ± 3.2			3.3 ± 3.2	2.7 ± 2.6		
Median [IQR]	4.0 [2.0-7.0]	3.0 [1.0-6.0]	0.001	*	4.0 [2.0-7.0]	3.0 [1.0-6.0]	0.015	*	2.0 [1.0-5.0]	2.0 [1.0-4.0]	0.132		2.0 [1.0-4.0]	2.0 [1.0-3.0]	0.019	*
ED visits																
Mean ± SD	3.0 ± 3.3	2.1 ± 1.5			2.8 ± 3.1	2.1 ± 1.6			2.1 ± 2.0	1.8 ± 1.1			2.3 ± 2.0	1.6 ± 1.0		
Median [IQR]	2.0 [1.0-3.0]	2.0 [1.0-2.3]	0.070		2.0 [1.0-3.0]	2.0 [1.0-2.0]	0.262		1.0 [1.0-2.0]	1.0 [1.0-2.0]	0.995		2.0 [1.0-2.0]	1.0 [1.0-2.0]	0.027	*
All-cause costs																
Total costs (medical + pharmacy)																
Mean ± SD	\$19,117 ± \$46,080	\$4056 ± \$9818			\$23,079 ± \$58,084	\$5878 ± \$25,355			\$13,542 ± \$38,556	\$3350 ± \$12,516			\$10,997 ± \$25,159	\$3924 ± \$16,379		
Median [IQR]	\$2642 [\$741-\$15,483]	\$680 [\$196-\$2236]	<0.001	*	\$770 [\$21,060]	\$1060 [\$3766]	<0.001	*	\$1998 [\$456-\$10,960]	\$736 [\$200-\$2590]	<0.001	*	\$1769 [\$286-\$10,379]	\$632 [\$186-\$2,011]	<0.001	*
Medical costs																
Mean ± SD	\$15,469 ± \$42,672	\$3441 ± \$8727			\$18,950 ± \$55,415	\$5149 ± \$25,057			\$11,592 ± \$37,873	\$2984 ± \$12,513			\$9279 ± \$23,867	\$3661 ± \$16,791		
Median [IQR]	\$2028 [\$667-\$8524]	\$645 [\$204-\$2065]	<0.001	*	\$2264 [\$621-\$14,127]	\$851 [\$299-\$3023]	<0.001	*	\$1397 [\$385-\$8150]	\$590 [\$174-\$1796]	<0.001	*	\$1022 [\$310-\$6108]	\$500 [\$214-\$1699]	0.001	*
Inpatient costs																
Mean ± SD	\$52,016 ± \$119,632	\$11,402 ± \$14,727			\$51,665 ± \$106,524	\$29,303 ± \$76,842			\$43,039 ± \$95,813	\$25,592 ± \$45,200			\$43,083 ± \$68,311	\$29,380 ± \$60,933		
Median [IQR]	\$4093 [\$994-\$4706]	\$4219 [\$2843-\$15,187]	0.721		\$9990 [\$3779-\$36,517]	\$4050 [\$1320-\$8672]	0.150		\$8339 [\$3779-\$27,276]	\$6456 [\$3398-\$18,857]	0.713		\$9990 [\$6301-\$42,048]	\$3173 [\$1430-\$3899]	0.143	
Outpatient costs																
Mean ± SD	\$9484 ± \$21,956	\$1640 ± \$3579			\$9925 ± \$22,028	\$2074 ± \$5306			\$5309 ± \$11,380	\$1239 ± \$2358			\$5767 ± \$11,943	\$1411 ± \$4321		
Median [IQR]	\$1519 [\$569-\$4454]	\$457 [\$161-\$1114]	<0.001	*	\$1461 [\$536-\$6107]	\$572 [\$216-\$1821]	<0.001	*	\$845 [\$295-\$3077]	\$431 [\$158-\$1113]	<0.001	*	\$843 [\$234-\$4198]	\$394 [\$175-\$1184]	<0.001	*
Lab/imaging visits																
Mean ± SD	\$779 ± \$1835	\$643 ± \$1117			\$861 ± \$2272	\$780 ± \$2089			\$534 ± \$1348	\$464 ± \$985			\$609 ± \$1293	\$675 ± \$2356		
Median [IQR]	\$303 [\$132-\$691]	\$208 [\$67-\$499]	0.058		\$322 [\$125-\$967]	\$210 [\$75-\$674]	0.065		\$214 [\$78-\$529]	\$141 [\$60-\$397]	0.167		\$268 [\$99-\$594]	\$123 [\$60-\$374]	0.043	*
ED costs																
Mean ± SD	\$5824 ± \$16,404	\$3358 ± \$8875			\$8871 ± \$19,816	\$2432 ± \$5768			\$7489 ± \$18,917	\$1296 ± \$2076			\$5485 ± \$14,307	\$2908 ± \$6956		
Median [IQR]	\$780 [\$301-\$1966]	\$717 [\$352-\$1422]	0.734		\$2200 [\$579-\$8358]	\$590 [\$341-\$1630]	0.002	*	\$1989 [\$358-\$6824]	\$627 [\$253-\$1014]	0.004	*	\$761 [\$403-\$2703]	\$453 [\$255-\$2184]	0.305	
Pharmacy costs																
Mean ± SD	\$5126 ± \$16,969	\$1438 ± \$6090			\$5838 ± \$11,409	\$1437 ± \$4974			\$3018 ± \$5976	\$763 ± \$2629			\$3469 ± \$7181	\$1011 ± \$3029		
Median [IQR]	\$576 [\$60-\$29,414]	\$83 [\$14-\$530]	<0.001	*	\$806 [\$100-\$4900]	\$150 [\$17-\$544]	<0.001	*	\$617 [\$95-\$29,414]	\$91 [\$14-\$330]	<0.001	*	\$653 [\$41-\$29,414]	\$74 [\$22-\$525]	0.001	*