



Economic and Clinical Burden of Diagnosed Congenital Cytomegalovirus Disease in France During the First 2 Years of Life

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BACKGROUND

- Congenital cytomegalovirus (cCMV) is the leading infectious cause of birth defects in infants born in high-income countries,^{1,2} with an estimated birth prevalence of 0.4% in France³
 - Approximately 1 in 5 infants with cCMV develop long-term health complications, including hearing loss, microcephaly, vision loss, and developmental/neurological effects^{1,4,5}
- Despite the considerable economic burden associated with cCMV, limited awareness persists,⁶ and lack of systematic surveillance precludes a full understanding of the burden^{5,7,8}
- Comprehensive analyses of the economic and clinical burden associated with cCMV in the general French population remain scarce

OBJECTIVE

- To assess healthcare resource utilization (HRU), direct costs, and cCMV-related clinical outcomes among infants diagnosed with cCMV in France in their first 2 years of life

METHODS

Study Design

- Retrospective study design utilizing healthcare claims data from the Système National des Données de Santé database (01/01/2015-31/12/2023)
- cCMV Cases: ≥ 1 diagnosis code for cCMV (ICD-10:P35.1) or cytomegalovirus (CMV; ICD-10:B25.x) within 1 month of birth; Controls: no diagnosis of cCMV or CMV at any point during follow-up
- Cases matched 1:1 to controls on birth year, sex, region of residence, and cCMV index year
- Study participants were required ≥ 2 years of follow-up after the index date
 - The cCMV index date was the first diagnosis of cCMV/CMV for cases and a randomly selected date from all claims within 1 month of birth for controls
- The cCMV cases were followed for first 2 years of life (observation period)
- Birth admission (ie the initial hospitalization at delivery) was analyzed separately to distinguish neonatal care from postnatal healthcare use during the 2-year observation period

Study Outcomes and Statistical Analyses

- All-cause HRU, direct costs, and relevant clinical events were captured
 - Inpatient admissions, emergency department visits, outpatient visits, pharmacy claims
 - Values for each HRU category were reported as the average total number of visits and average total costs among patients with ≥ 1 visit during the observation period
 - cCMV-related sequelae were selected *a priori* by clinical experts: hearing loss, vision impairment, cerebral palsy, developmental and motor delays, congenital malformations of the nervous system, hemorrhagic conditions, immune disorders, liver-related conditions, and sleeping disturbances
- Comparisons between matched cases and controls were conducted using Wilcoxon rank sum test for continuous variables and chi-square test for categorical variables

RESULTS

Patient Characteristics

- Our cohort comprised 1,434 matched pairs of diagnosed cCMV cases and non-cCMV controls (Table 1)

Table 1. Patient characteristics among matched diagnosed cCMV cases and non-cCMV controls

Characteristics at index	Cases N = 1,434	Controls N = 1,434
Age (months), mean \pm SD	0.1 \pm 0.2	0.3 \pm 0.3
Male, n (%)	728 (50.8)	728 (50.8)
Insurance type, n (%)		
Universal health insurance	1,175 (81.9)	1,226 (85.5)
CMU-c, ACS or C2S	250 (17.4)	204 (14.2)
AME	9 (0.6)	4 (0.3)
Unknown	0 (0.0)	0 (0.0)
First cCMV/CMV diagnosis, n (%)		
cCMV	1,252 (87.3)	0 (0.0)
CMV	149 (10.4)	0 (0.0)
Both cCMV and CMV	33 (2.3)	0 (0.0)
Follow-up period duration, years		
Mean \pm SD	5.3 \pm 2.0	5.2 \pm 2.0
Median [IQR]	5.2 [3.6–7.0]	5.2 [3.6–6.9]

ACS, Aide à l'acquisition d'une complémentaire santé; AME, Aide médicale de l'État; C2S, Complémentaire Santé Solidarité; cCMV, congenital cytomegalovirus; CMU-c, couverture maladie universelle complémentaire; CMV, cytomegalovirus; IQR, interquartile range; SD, standard deviation.

All-Cause HRU

- During the observation period, diagnosed cCMV cases had significantly higher mean number of medical visits than controls, and were significantly more likely to have ≥ 1 inpatient admissions (Table 2)
 - Birth admissions were captured in 93.9% of cases and 74.5% of controls
 - On average, diagnosed cCMV cases had significantly longer birth admission length of stay than controls (mean: 24.6 vs. 6.4 days; $p < 0.001$)

Table 2. All-cause HRU during the observation period

All-cause HRU ¹	Year 1			Year 2		
	Cases N = 1,434	Controls N = 1,434	P-value	Cases N = 1,434	Controls N = 1,434	P-value
	Proportion of patient with any visit, n (%)					
Total visits	1,424 (99.3%)	1,421 (99.1%)	0.53	1,413 (98.5%)	1,408 (98.2%)	0.46
Inpatient admissions²	679 (47.4%)	291 (20.3%)	< 0.001*	372 (25.9%)	210 (14.6%)	< 0.001*
ED visits	602 (42.0%)	488 (34.0%)	< 0.001*	441 (30.8%)	375 (26.2%)	0.006*
Outpatient visits	1,423 (99.2%)	1,415 (98.7%)	0.14	1,410 (98.3%)	1,399 (97.6%)	0.15
Pharmacy claims	1,414 (98.6%)	1,417 (98.8%)	0.62	1,402 (97.8%)	1,407 (98.1%)	0.51
All-cause HRU among patients with ≥ 1 visit						
Total visits						
Mean \pm SD	33.7 \pm 37.0	18.9 \pm 20.6	< 0.001*	22.6 \pm 36.3	12.5 \pm 18.2	< 0.001*
Median [IQR]	22.0 [14.5–36.0]	15.0 [10.0–21.0]		12.0 [7.0–21.0]	9.0 [5.0–13.0]	
Inpatient admissions²						
Mean \pm SD	1.9 \pm 1.7	3.1 \pm 13.8	< 0.001*	1.9 \pm 2.1	3.7 \pm 16.0	0.001*
Median [IQR]	1.0 [1.0–2.0]	1.0 [1.0–2.0]		1.0 [1.0–2.0]	1.0 [1.0–1.0]	
ED visits						
Mean \pm SD	3.0 \pm 8.0	2.1 \pm 1.9	0.05	2.3 \pm 2.9	2.5 \pm 5.5	0.11
Median [IQR]	2.0 [1.0–3.0]	1.0 [1.0–2.0]		1.0 [1.0–3.0]	1.0 [1.0–2.0]	
Outpatient visits						
Mean \pm SD	31.5 \pm 35.9	17.6 \pm 18.8	< 0.001*	21.4 \pm 35.7	11.3 \pm 15.6	< 0.001*
Median [IQR]	21.0 [13.0–34.0]	14.0 [10.0–20.0]		11.0 [7.0–20.0]	8.0 [5.0–12.0]	

cCMV, congenital cytomegalovirus; CMV, cytomegalovirus; ED, emergency department; HRU, healthcare resource utilization; IQR, interquartile range; SD, standard deviation.

[1] All HRU were summarized only among patients with that type of HRU during the first and second year of life.

[2] Inpatient admissions excluded the birth admission for each patient.

All-Cause Direct Costs

- Diagnosed cCMV cases had significantly higher birth admission costs, as well as medical costs, than controls in post-index Year 1 and Year 2 (Figure 1)

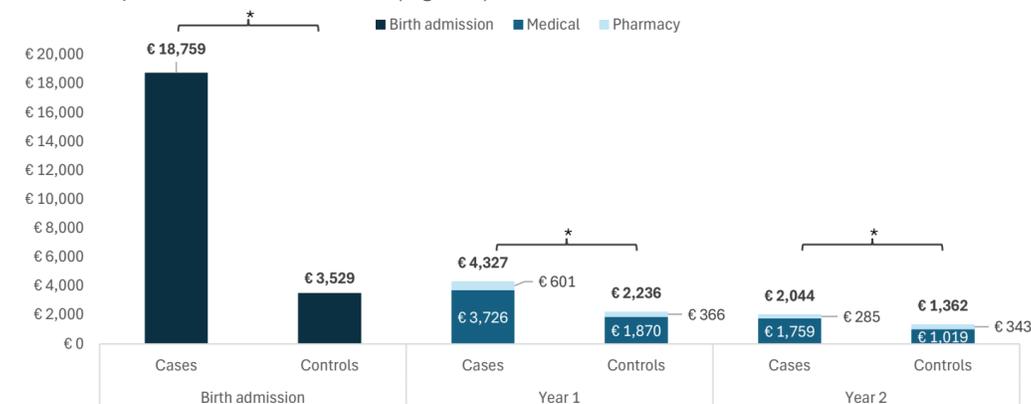


Figure 1. All-cause direct costs (reported in 2023 euro (€)) during the birth admission and the observation period

cCMV-Related Sequelae

- Diagnosed cCMV cases experienced significantly more potentially cCMV-related clinical events than controls during the observation period (45.7% vs. 8.4%)
 - The most common clinical events potentially related to cCMV among cases were liver-related conditions, hemorrhagic conditions, and congenital malformations and disorders of the nervous system (Figure 2)

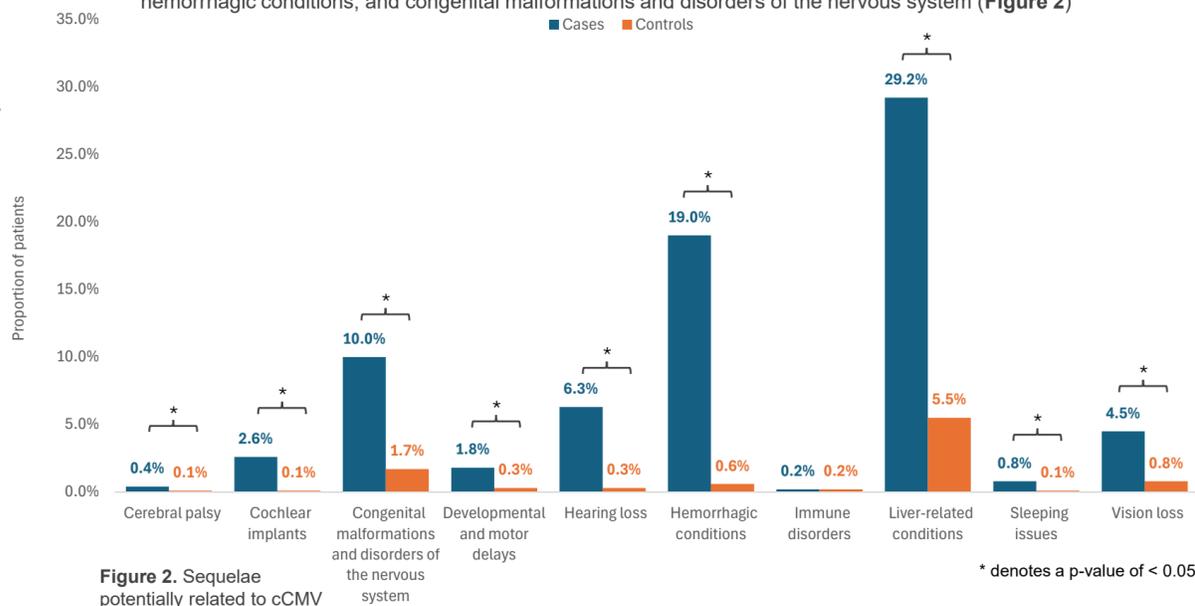


Figure 2. Sequelae potentially related to cCMV * denotes a p-value of < 0.05

CONCLUSIONS

- In France, infants with diagnosed cCMV had significantly higher HRU and costs and experienced worse clinical outcomes during the first 2 years of life compared with controls
 - Inpatient care, including birth admissions, contributed substantially to the cost burden
- As early identification enables timely treatment and developmental monitoring, interventions and policies to increase early screening of cCMV are needed to mitigate the associated economic and clinical burden
- Future studies should investigate longer-term costs beyond the first 2 years of life, as well as the indirect and societal costs associated with cCMV in France
- Study limitations include potential underestimation of diagnoses and procedures due to coding inaccuracies, exclusion of undiagnosed cCMV cases among controls, and omission of indirect or out-of-pocket costs

Additional Information

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

Disclosures

This research was funded by ModernaTX, Inc. PB and JD-D are employees of ModernaTX, Inc. and own stock/stock options. NK and UD are employees of and MC, KC, KG and VL are former employees of Analysis Group, Inc., which received support from ModernaTX, Inc. for conducting this research.

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