

THE INCREMENTAL ECONOMIC BURDEN OF CONGENITAL CYTOMEGALOVIRUS IN THE FIRST YEAR OF LIFE:

A Retrospective Case-Control Analysis of Medicaid and Commercial Health Insurance Claims Data

Tuesday September 25, 2018

Juliana Meyers,¹ **Anushua Sinha**,² Salome Samant,² Laurel Trantham,¹ Sean Candrilli¹

¹ RTI Health Solutions; ² Merck & Co., Inc., Kenilworth, NJ, USA

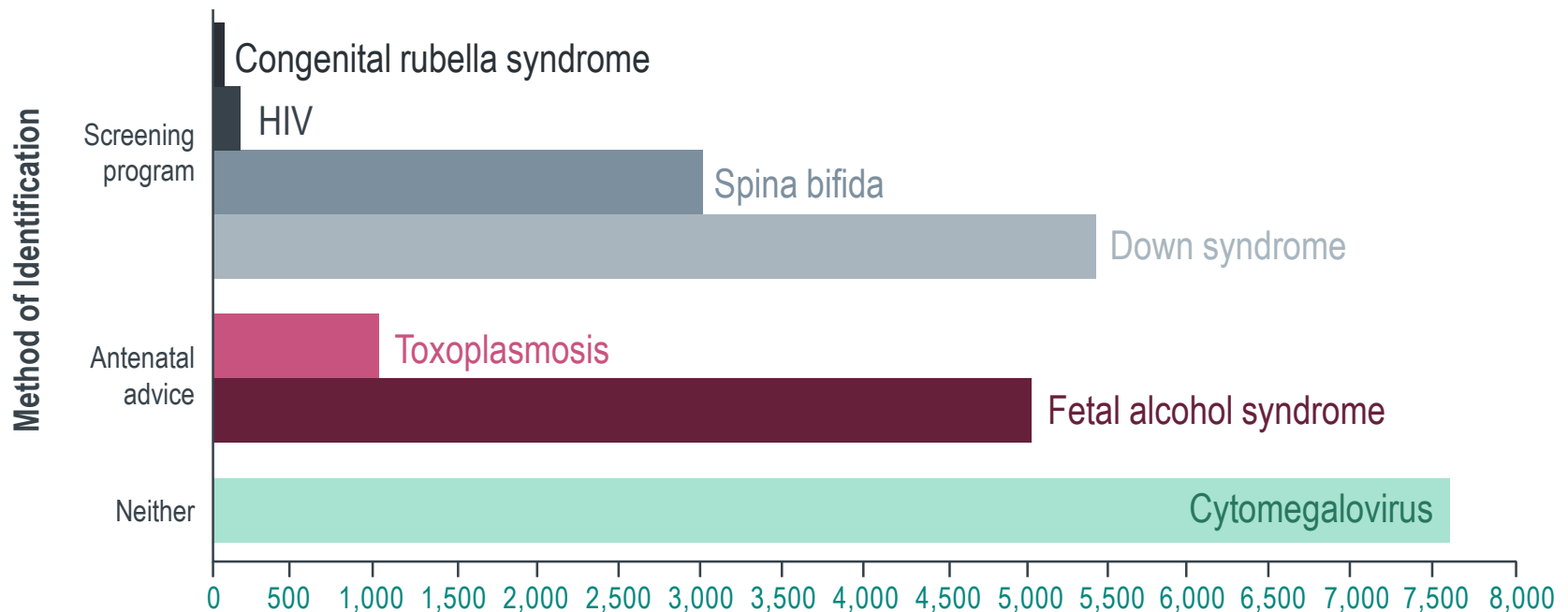
Presented at the 2018 CMV Public Health and Policy Conference

Disclosures

I am a full-time employee of Merck & Co., with stock holdings. Funding was provided to RTI Health Solutions for the conduct of the study.

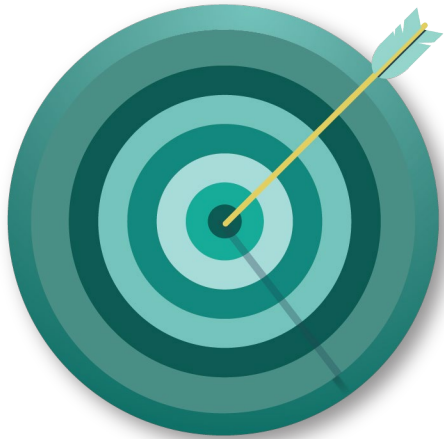
Background and Rationale

Annual cases of congenital diseases in the US



- Congenital cytomegalovirus (cCMV) causes a heavy burden of infant and childhood disease.
- Limited evidence exists that describe the economic burden associated with cCMV disease in the US.

Objective



To assess the incremental health care resource use and costs of cCMV at birth and during the first year of life in the United States, by comparing infants with and without a diagnosis of cCMV in a large, nationally representative data set.

Data Source: IBM Watson MarketScan Research Databases¹

	MarketScan Commercial Claims and Encounters (CCAЕ)	MarketScan Multistate Medicaid (Medicaid)
Population	Patients covered under fee-for-service and capitated health plans	Medicaid enrollees from geographically dispersed states
Period	January 2011 to December 2016	January 2011 to December 2015
Data availability	<ul style="list-style-type: none"> • Inpatient, outpatient, and pharmacy claims plus demographic and enrollment details • Medical claims included information on place of service, ICD-9-CM/ICD-10-CM diagnosis and procedure codes, dates of service, paid amounts 	
cCMV case definition	Identified based on presence of an ICD-9-CM/ICD-10-CM diagnosis code for cCMV	
Institutional review board	Study data were de-identified, retrospective, and collected for administrative purposes. RTI International’s institutional review board determined that this study was exempt.	
Results	Results were pooled across the databases.	

¹ <https://truvenhealth.com/markets/life-sciences/products/data-tools/marketscan-databases>

Study Design: Overview

Stage 1: Birth Analysis



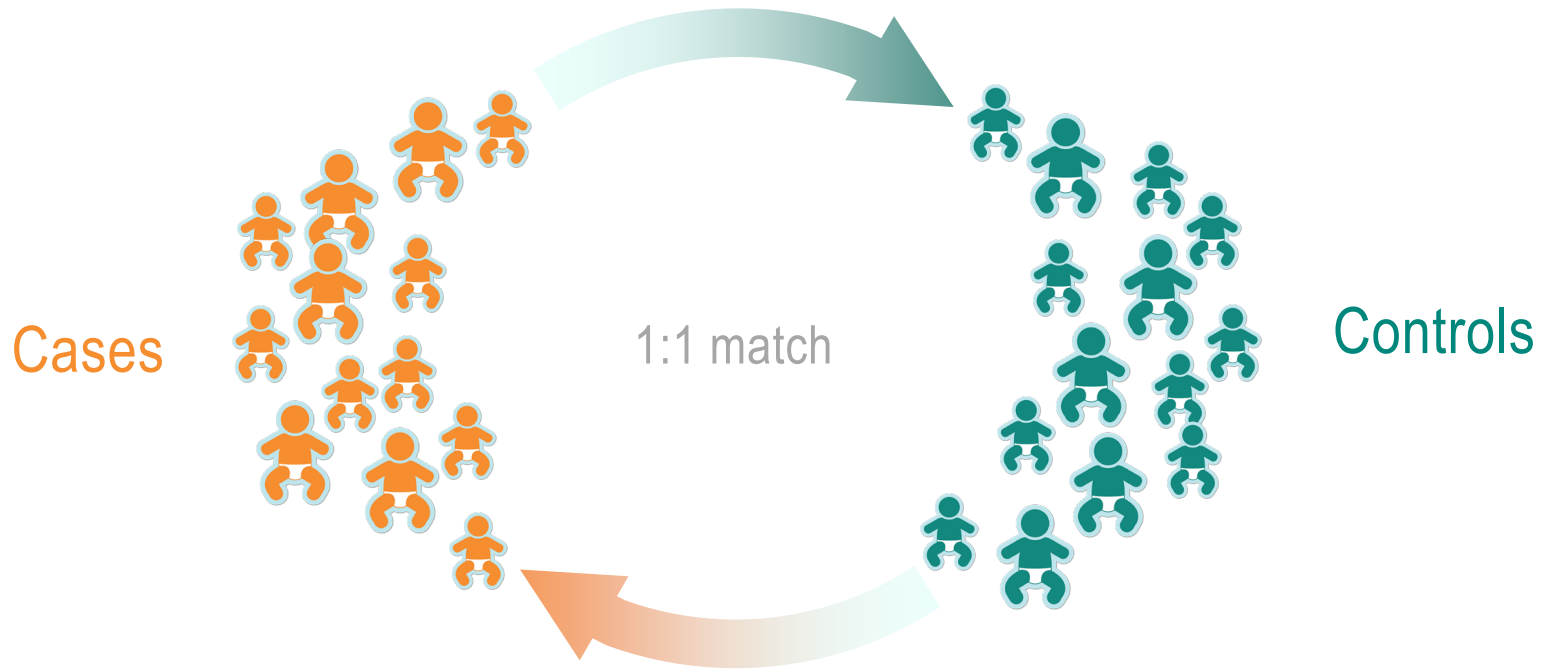
Reported on length of stay and costs during the birth admission

Stage 2: Post-Birth Analysis



Reported on health care resource utilization and costs during the first year of life (excluding the birth admission)

Study Design: Case-Control



In both Stage 1 (Birth Analysis) and Stage 2 (Post-Birth Analysis) infants with cCMV were matched to infants without cCMV based on demographic and clinical characteristics: sex, vaginal or Caesarian delivery, race, health plan type, region, payer type, birth weight category, and gestational age.

Study Design: Patient Selection and Matching

Stage 1: Birth Analysis

Admissions designated as “maternal and newborn admissions”

Birth occurred

Newborn only

cCMV diagnosis

No cCMV diagnosis

1:1 match



Stage 2: Post-Birth Analysis

Continuous health plan enrollment for 12 months post-index date

cCMV diagnosis, age < 1 year at 1st cCMV diagnosis

No cCMV diagnosis

No HIV, SOT, hematopoietic stem cell transplant diagnosis

1:1 match



Study Design: Outcome Measures

Stage 1: Birth Analysis

- Length of stay (LOS) and costs for the admission
- Incremental LOS and costs of cCMV at birth calculated as the difference in LOS and costs between cCMV cases and non-cCMV controls

Stage 2: Post-Birth Analysis

- All-cause and cCMV-related health care resource utilization (HCRU) and costs
- Incremental resource utilization and costs of cCMV calculated as the difference between cCMV cases and matched non-cCMV controls
- cCMV-related care included:
 - Inpatient visits with a primary diagnosis of cCMV
 - Outpatient visits with any diagnosis of cCMV
 - Pharmacy claims for ganciclovir or valganciclovir

Results: Cases and Controls

Stage 1: Birth Analysis

Admissions designated as “maternal and newborn admissions”

N = 2,759,479

Newborn only
N = 2,548,971

cCMV diagnosis
N = 404

No cCMV diagnosis
N = 2,548,514



1:1 match



Stage 2: Post-Birth Analysis

N = 3,711,896

Continuous health plan enrollment for 12 months post-index date

cCMV diagnosis, age < 1 year at 1st cCMV diagnosis
N = 679

No cCMV diagnosis
N = 1,792,739

No HIV, SOT, hematopoietic stem cell transplant diagnosis
N = 1,791,493



1:1 match



Results: cCMV Population Characteristics

Characteristic		Stage 1: Birth Analysis	Stage 2: Post-Birth Analysis
Total		404	679
Payer	Commercial	170 (42.1%)	219 (32.3%)
	Medicaid	234 (58.0%)	460 (67.8%)
Sex	Male	198 (49.0%)	368 (54.2%)
	Female	199 (49.3%)	309 (45.5%)
Weight	≤ 2,500 g	188 (46.5%)	230 (33.9%)
	> 2,500 g	16 (4.0%)	28 (4.1%)
	Missing	200 (49.5%)	421 (62.0%)
Gest. age	< 35 weeks	144 (35.6%)	157 (23.1%)
	35-36 weeks	48 (11.9%)	59 (8.7%)
	≥ 37 weeks	62 (15.3%)	99 (14.6%)
	Other immaturity	61 (15.1%)	—
	Unspecified	119 (29.5%)	364 (53.6%)

Gest. = gestational.

Results: Birth Analysis, Cases and Controls

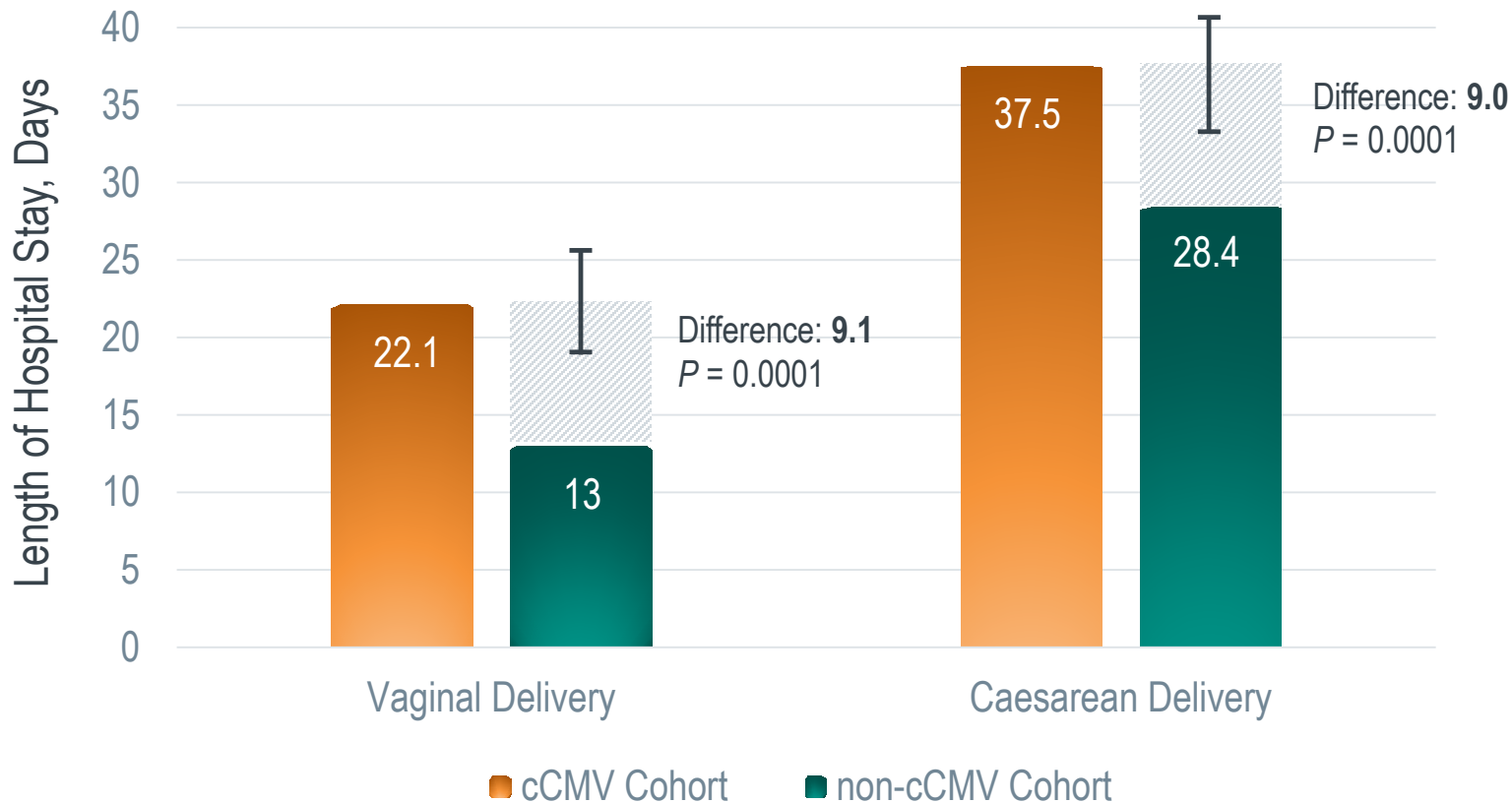
Characteristic		Vaginal Delivery		C-section Delivery	
		cCMV Cohort	Non-cCMV Cohort	cCMV Cohort	Non-cCMV Cohort
Total		170	1,717,801	234	737,721
Payer	Commercial	67 (39.4%)	863,658 (50.3%)	103 (44.0%)	413,128 (56.0%)
	Medicaid	103 (60.6%)	854,143 (49.7%)	131 (56.0%)	324,593 (44.0%)
Sex	Male	75 (44.1%)	831,929 (48.4%)	123 (52.6%)	369,400 (50.1%)
	Female	92 (54.1%)	856,455 (49.9%)	107 (45.7%)	355,663 (48.2%)
Weight	≤ 2,500 g	53 (31.2%)	57,398 (3.4%)	135 (57.7%)	58,741 (8.0%)
	> 2,500 g	6 (3.5%)	46,006 (2.7%)	10 (4.3%)	29,488 (4.0%)
	Missing	111 (65.3%)	1,614,397 (94.0%)	89 (38.0%)	649,492 (88.1%)
Gest. age	< 35 weeks	25 (14.7%)	33,923 (2.0%)	89 (38.0%)	38,681 (5.3%)
	35-36 weeks	18 (10.6%)	57,649 (3.4%)	30 (12.8%)	37,089 (5.0%)
	≥ 37 weeks	37 (21.8%)	129,636 (7.6%)	25 (10.7%)	66,894 (9.1%)
	Other immaturity	22 (12.9%)	17,988 (1.1%)	39 (16.7%)	18,805 (2.6%)
	Unspecified	68 (40.0%)	1,478,605 (86.1%)	51 (21.8%)	576,252 (78.1%)

Gest. = gestational.

Results: Post-Birth Analysis, Cases and Controls

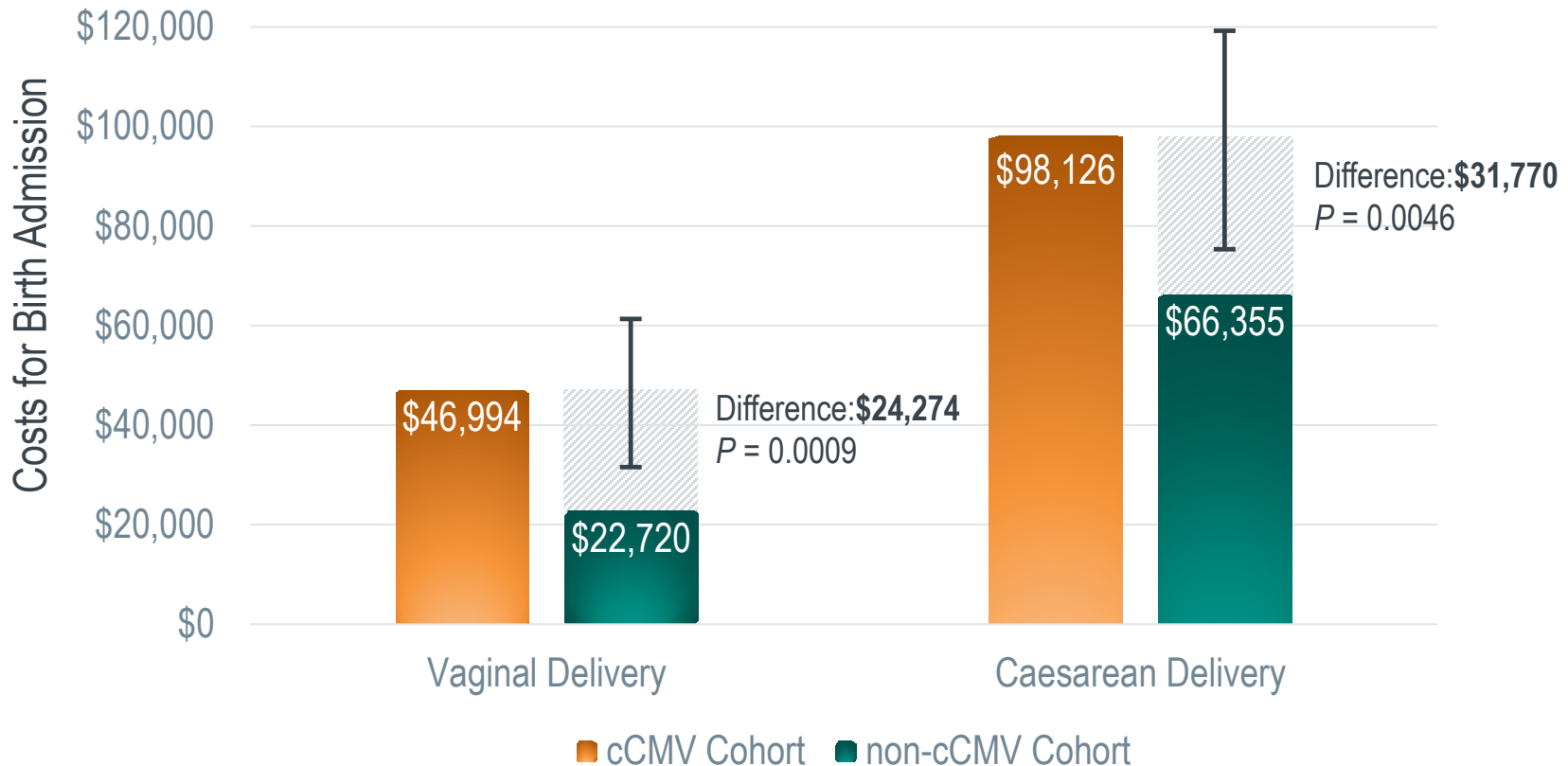
Characteristic		cCMV Cohort	Non-cCMV Cohort
Total		679	1,791,493
Payer	Commercial	219 (32.3%)	789,908 (44.1%)
	Medicaid	460 (67.8%)	1,001,585 (55.9%)
Sex	Male	368 (54.2%)	915,339 (51.1%)
	Female	309 (45.5%)	872,761 (48.7%)
Weight	≤ 2,500 g	230 (33.9%)	88,093 (4.9%)
	> 2,500 g	28 (4.1%)	50,330 (2.8%)
	Missing	421 (62.0%)	1,650,508 (92.1%)
Gest. age	< 35 weeks	157 (23.1%)	60,328 (3.4%)
	35-36 weeks	59 (8.7%)	63,347 (3.5%)
	≥ 37 weeks	99 (14.6%)	135,063 (7.5%)
	Other immaturity	—	—
	Unspecified	364 (53.6%)	1,532,755 (85.6%)

Birth Analysis: LOS for the Birth Admission



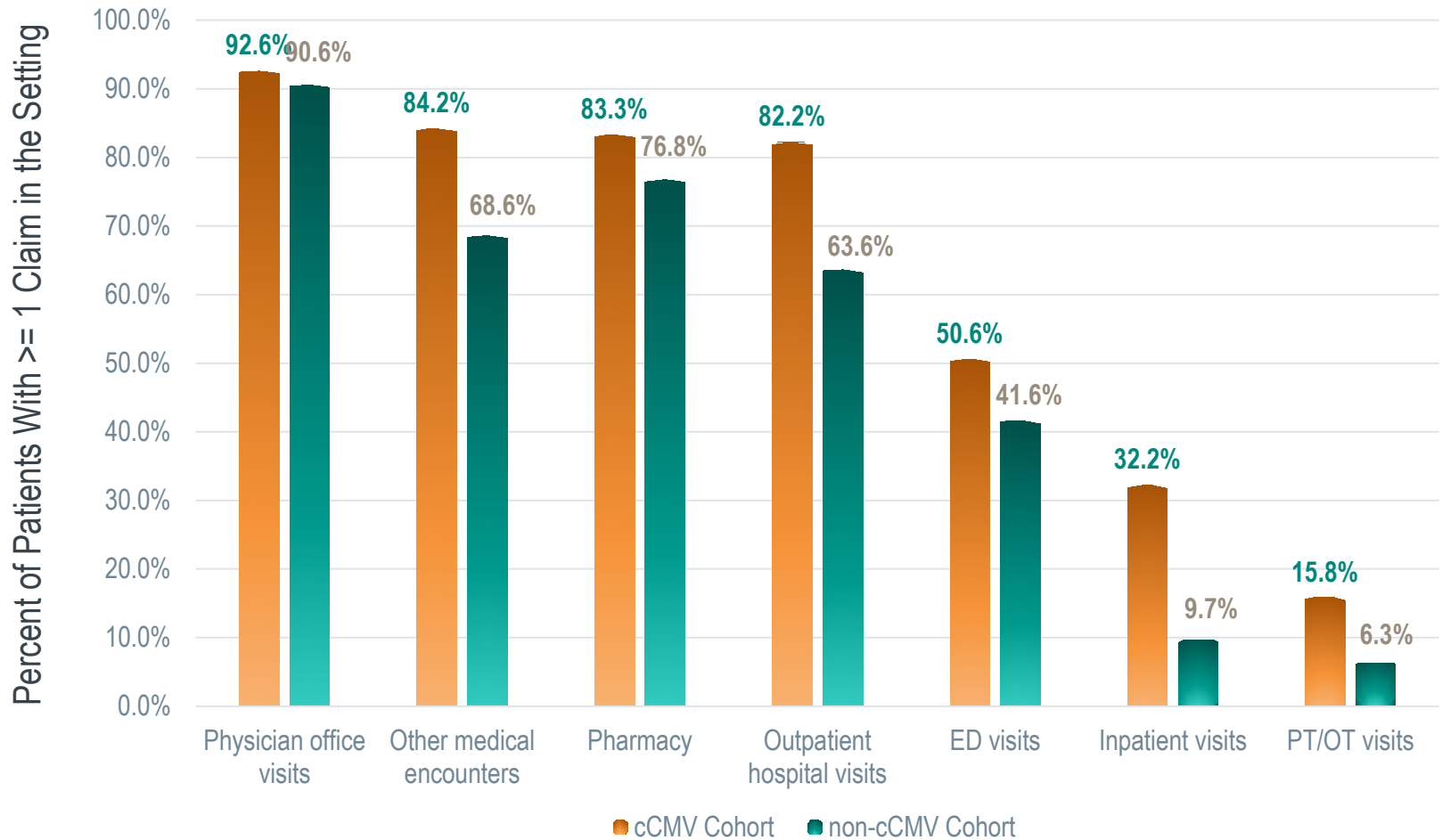
- cCMV was associated with a 70% increase in LOS among vaginal deliveries and a 30% increase in LOS among Caesarean deliveries.

Birth Analysis: Costs for the Birth Admission



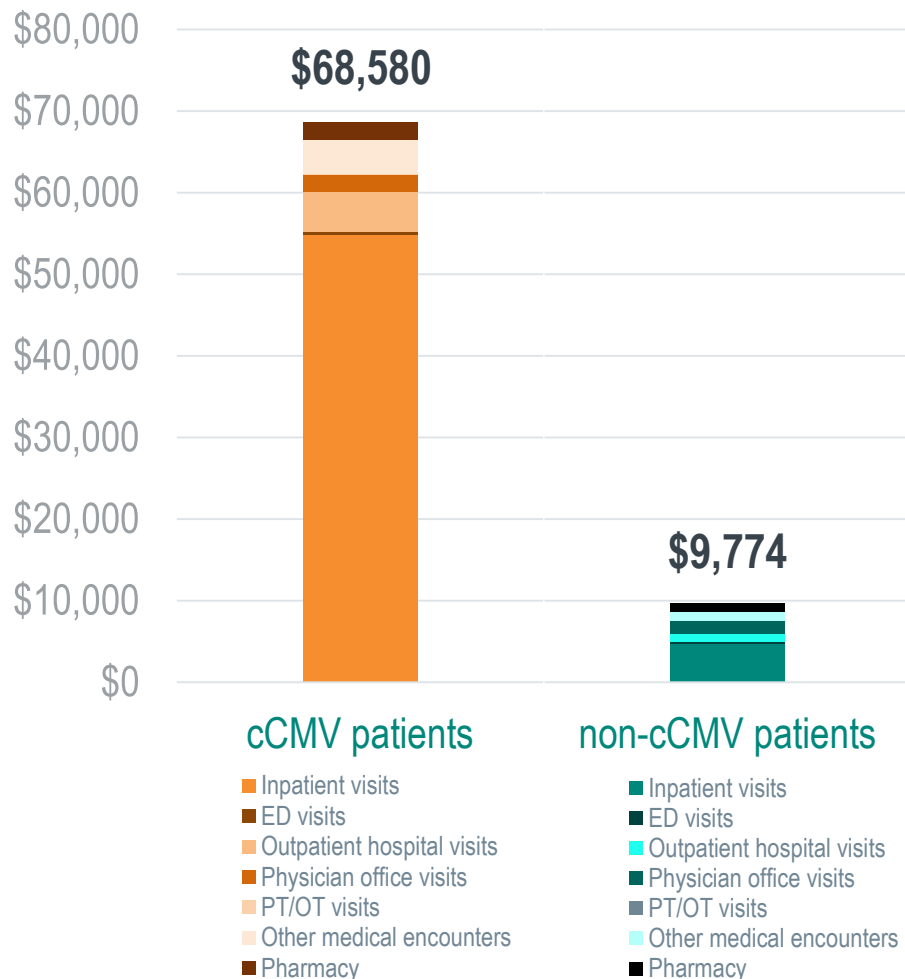
- cCMV was associated with a greater than 100% increase in costs among vaginal deliveries and a 48% increase in costs among Caesarean deliveries.

Post-Birth Analysis: All-Cause Resource Use



ED = emergency department; OT = occupational therapy; PT = physical therapy.

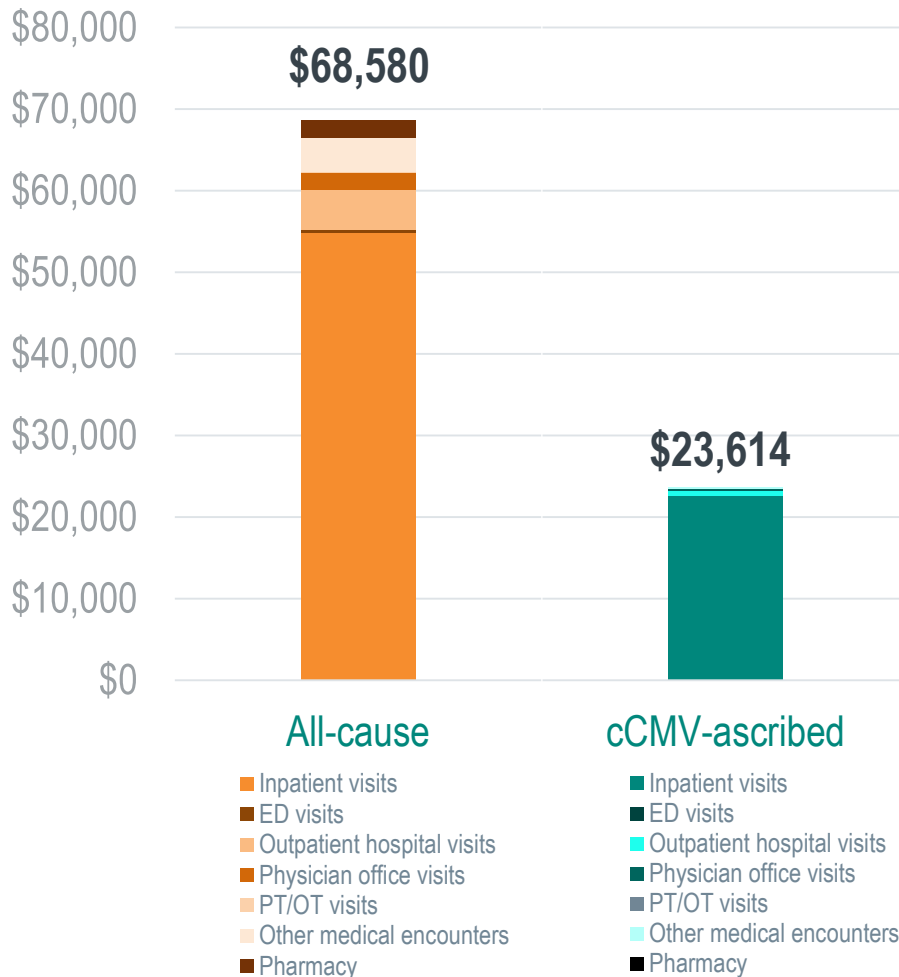
Post-Birth Analysis: All-Cause Costs



- During the first year of life, patients with cCMV accrued costs averaging 7 times greater than those of matched non-cCMV controls.
- Inpatient visits were responsible for over 85% of the difference in costs between patients with cCMV and non-cCMV controls.

$P < 0.0001$; 95% CI, \$41,247-\$76,365.

Post-Birth Analysis: Unadjusted cCMV-Ascribed Costs



- cCMV-ascribed inpatient costs represented over 95% of total cCMV-related costs.¹
- cCMV-ascribed costs represented approximately 34% of all-cause costs.

¹ cCMV-related inpatient visits were identified based on a primary diagnosis of cCMV.

Limitations

- Diagnoses were taken from administrative billing records, which are subject to miscoding or undercoding, and no clinical or electronic medical records were available to confirm diagnoses or clinical events.
- It was not possible to link infants with their mothers, and infant birth costs may have been accrued on the mothers' insurance.
 - To mitigate this limitation, we conducted a two-stage approach to evaluating the burden of cCMV.
- Infants with cCMV who were asymptomatic at birth and during their first year of life were not included in the analysis.
- Costs were based on health plan–paid amounts, which only reflect the costs incurred by payers and do not capture other costs associated with cCMV.

Conclusions

- cCMV is associated with a substantial economic burden both at birth and throughout the first year of life.
 - At birth, patients with cCMV accrued health care costs that averaged 1.5 and 2.1 times greater than those of matched non-cCMV controls for Caesarean and vaginal delivery, respectively.
 - During the first year of life, patients with cCMV had costs that were, on average, 7 times greater than those of matched patients without cCMV.
- Although the numbers are substantial, this finding may represent a fraction of the total burden that children with cCMV will face during their lifetime.
 - Future research to evaluate the burden of cCMV beyond the first year of life is needed.

BACK-UP SLIDES

Data Source

- This study used two IBM Watson MarketScan Research Databases.
- MarketScan Commercial Claims and Encounters (CCAE) database: includes patients covered under a variety of fee-for-service and capitated health plans with more than 47 million covered lives captured in 2014.
- MarketScan Multistate Medicaid (Medicaid) database: includes more than 28 million Medicaid enrollees in geographically dispersed states.
- Both databases included information on inpatient, outpatient, and pharmacy claims as well as demographic and enrollment details.
- Medical claims included information on place of service, ICD-9-CM/ICD-10-CM diagnosis and procedure codes, dates of service, and paid amounts.
- Data spanned January 2011 to December 2016 for the CCAE database and January 2011 to December 2015 for the Medicaid database.
- All results were pooled across the databases.
- As study data were de-identified, retrospective, and collected for administrative purposes, RTI International's institutional review board determined that this study was exempt from review.

Patient Selection Criteria and Matching: Birth Analysis

- Admissions designated as “maternal and newborn admissions” based on an admission type variable provided by the vendor
- Patients were further required to have a diagnosis code on the admission indicating a birth had occurred.¹
- Admissions were further required to be for newborns only (i.e., admission records with mothers’ and infants’ information on the same claim were excluded) based on either of the following criteria:
 - Patient aged 0 years at the time of admission.
 - Admissions with a patient aged greater than 0 years with no diagnosis code for the mother’s stay.²

¹ ICD-9-CM diagnosis code V29-V39; ICD-10-CM diagnosis code Z38 or Z05.

² ICD-9-CM code V27; ICD-10-CM diagnosis code Z37.

Patient Selection Criteria and Matching: Birth Analysis

- Infant admissions with a cCMV diagnosis (i.e., the cCMV cohort) were identified based on a corresponding diagnosis during the inpatient stay.¹
 - Infant admissions were included in the non-cCMV cohort if the infant did not have a diagnosis of cCMV during the inpatient stay.
- Admissions for the cCMV cohort were matched 1:1 to admissions in the non-cCMV cohort using a direct covariate-matching approach.
 - Sex of the newborn, birth type (i.e., vaginal or Caesarian), race, health plan type, region, payer type, birth weight category, and gestational age at birth category were used to match cases and controls.
 - Matches were selected at random if more than one control was available.

¹ ICD-9-CM diagnosis codes 771.1 or 078.5; ICD-10-CM diagnosis code P35.1 or B25.

Patient Selection Criteria and Matching: Post-Birth Analysis

- Infants were included in the cCMV cohort if they had at least 1 medical claim with a cCMV diagnosis¹ and were younger than 1 year on the date of the first observed claim for cCMV.
 - The date of the first observed medical claim (cCMV or otherwise) defined the index date.
 - Infants were required to have continuous medical and pharmacy enrollment for a minimum follow-up period of 12 months.
- Infants were included in the non-cCMV cohort if they had no medical claims with a diagnosis of cCMV during the first year of life.
 - The date of the first observed medical claim defined the index date.
 - Infants were required to have continuous medical and pharmacy enrollment for a minimum follow-up period of 12 months.
- Infants with a diagnosis of HIV, solid organ transplant, or stem cell transplant were excluded from the analysis, as they could have been at risk of invasive CMV due to immunodeficiency.

¹ ICD-9-CM diagnosis code 771.1 or 078.5; ICD-10-CM diagnosis code P35.1 or B25.

Patient Selection Criteria and Matching: Post-Birth Analysis

- Infants in the cCMV cohort were matched 1:1 to infants in the non-cCMV cohort using direct covariate matching.
 - The same list of covariates used in the birth analysis was employed (excluding birth type).
 - If more than one match was available for a case, the control was selected at random.

Adjusted LOS & Costs – Birth Analysis

	LOS	Costs
Vaginal delivery		
cCMV admissions, mean (SD)	20.5 (4.4)	\$39,561 (\$13,891)
Non-cCMV admissions, mean (SD)	14.6 (1.6)	\$23,993 (\$4,537)
Difference, mean (SD); 95% CI; <i>P</i> value	5.9 (4.6); 5.2-6.6; < 0.0001	\$15,568 (\$14,498); \$13,353-\$17,783; < 0.0001
Caesarean delivery		
cCMV admissions, mean (SD)	38.6 (8.4)	\$93,008 (\$32,755)
Non-cCMV admissions, mean (SD)	27.3 (3.3)	\$55,809 (\$12,376)
Difference, mean (SD); 95% CI; <i>P</i> value	11.4 (9.0); 10.2-12.5; < 0.0001	\$37,199 (\$34,663); \$32,696-\$41,703; < 0.0001

- Multivariable analyses were conducted to control for characteristics (i.e., comorbidities) not included in the match.¹
- It was observed that data were extremely right-skewed (as is common in cost data); therefore, cost values greater than \$500,000 (i.e., approximately 95th percentile of the cost distribution) were set equal to \$500,000 (i.e., “Winsorizing”).

¹ Included disorders relating to short gestation and low birth weight, other respiratory infections, symptoms concerning nutrition and metabolic development, other diseases of the lung, and other congenital anomalies of the circulatory system.

Adjusted LOS & Costs – Post-Birth Analysis

	Mean (SD)
Inpatient Services	
cCMV patients	\$56,610 (\$109,028)
Non-cCMV patients	\$3,552 (\$8,968)
Difference ²	\$53,058 (\$107,040); \$44,986-\$61,129; < 0.0001
Outpatient Hospital Visits	
cCMV patients	\$4,900 (\$4,669)
Non-cCMV patients	\$1,104 (\$1,133)
Difference ²	\$3,796 (\$4,552); \$3,453-\$4,140; < 0.0001
Other Medical Encounters	
cCMV patients	\$4,675 (\$6,652)
Non-cCMV patients	\$1,034 (\$1,872)
Difference ²	\$3,642 (\$6,313); \$3,165-\$4,118; < 0.0001
Total Costs	
cCMV patients	\$48,540 (\$73,025)
Non-cCMV patients	\$9,449 (\$17,452)
Difference ²	\$39,091 (\$70,554); \$33,771-\$44,411; < 0.0001

- Multivariable analyses were conducted to control for characteristics (i.e., comorbidities) not included in the match.¹
- It was observed that data were extremely right-skewed (as is common in cost data); therefore, cost values greater than \$500,000 (i.e., approximately 95th percentile of the cost distribution) were set equal to \$500,000 (i.e., “Winsorizing”).

¹ Included disorders relating to short gestation and low birth weight, other respiratory infections, symptoms concerning nutrition and metabolic development, other diseases of the lung, and other congenital anomalies of the circulatory system.

² Mean (SD); 95% CI; *P* value.