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Valganciclovir use among commercially and Medicaid-insured infants with congenital CMV infection in the United States, 2009–2015

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Abstract

Purpose—To assess clinical characteristics and trends in valganciclovir use among infants diagnosed with congenital cytomegalovirus (CMV) disease in the United States.

Methods—We analyzed 2009–2015 medical claims from Truven Health MarketScan® Commercial Claims and Encounters and Medicaid databases. We identified infants with a live birth code in the first claim who were enrolled for at least 45 days. Among infants diagnosed with congenital CMV disease, identified by an ICD-9-CM or ICD-10-CM code of congenital CMV infection or CMV disease within 45 days of birth, we assessed codes for CMV-associated clinical condition within the same period, and hearing loss and valganciclovir claims within the first 180 days.

Findings—In the commercial and Medicaid databases, we identified 257 (2.5/10,000) and 445 (3.3/10,000) infants diagnosed with congenital CMV disease, respectively, among whom 135 (53%) and 282 (63%) had ≥1 CMV-associated condition, 30 (12%) and 32 (7%) had hearing loss, and 41 (16%) and 78 (18%) had valganciclovir claims. Among infants with congenital CMV disease who had valganciclovir claims, 37 (90%) among commercially-insured infants and 68 (87%) among Medicaid-insured infants had ≥1 CMV-associated condition and/or hearing loss.

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CONTIBUTOR'S STATEMENT PAGE

J.L. designed the study, analyzed and interpreted the data, drafted the initial manuscript, and reviewed and revised the manuscript.
S.D. proposed the study, designed the study, interpreted the data, and critically reviewed the manuscript.
S.D.G. designed the study, interpreted the data, and critically reviewed the manuscript.
W.C. designed the study, interpreted the data, and critically reviewed the manuscript.
T.D. designed the study, interpreted the data, and critically reviewed the manuscript.
M.P. designed the study, interpreted the data, and critically reviewed the manuscript.
T.L. designed the study, interpreted the data, critically reviewed the manuscript, and supervised the project.
All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

From 2009 to 2015, the proportion with valganciclovir claims increased from 0% to 29% among commercially-insured infants and from 4% to 37% among Medicaid-insured infants (p<0.0001).

Implications—During 2009–2015, there was a strong upward trend in valganciclovir claims among insured infants who were diagnosed with congenital CMV disease, the majority of whom had CMV-associated conditions and/or hearing loss.

Keywords

CMV; cytomegalovirus; congenital; antiviral; valganciclovir; MarketScan

INTRODUCTION

Cytomegalovirus (CMV) is one of the most common congenital infections and can cause sensorineural hearing loss (SNHL), cognitive delays, and cerebral palsy[1]. The prevalence of congenital CMV infection in the United States is estimated to be 0.5%[2]. Approximately 10–15% of infected infants present with symptomatic disease at birth, which may include microcephaly, hepatosplenomegaly, petechiae, chorioretinitis, and jaundice[3]. Infants with symptomatic congenital CMV disease are also more likely to present with SNHL at birth or later, as well as cognitive delays and motor impairments[3, 4]. Most cases of symptomatic congenital CMV disease are likely undiagnosed in part because symptoms at birth are non-specific, and laboratory diagnosis must be performed within the first 3 weeks of life[1].

The first pilot study examining the use of intravenous (IV) ganciclovir for treatment of infants with symptomatic congenital CMV disease was published in 1994[5]. In 2003, data from a phase III trial of IV ganciclovir use for 6 weeks showed improved hearing and neurodevelopmental outcomes in treated infants, though treatment was associated with higher rates of neutropenia[6, 7]. Subsequent studies assessed the effect of the oral pro-drug valganciclovir[8, 9]. In 2012, the American Academy of Pediatrics (AAP) recommended that ganciclovir and valganciclovir treatment should be limited to neonates with symptomatic congenital CMV disease with central nervous system (CNS) involvement who were able to start treatment within the first month of life[10]. In 2015, the AAP reviewed the antiviral treatment recommendation based on data from a phase III trial of 6-month vs. 6-week treatment with valganciclovir for infants with symptomatic congenital CMV disease with or without CNS involvement that showed modest improvement of hearing and neurodevelopmental outcomes at 24 months, and a lower rate of neutropenia than seen in the study with IV ganciclovir[9, 11].

The extent to which antivirals are used for treatment of infants with symptomatic congenital CMV disease in the United States is unknown. We assessed clinical characteristics and trends in valganciclovir use among infants diagnosed with congenital CMV disease in the United States during 2009–2015 using a large national healthcare claims database.

METHODS

Data Source

We used 2 Truven Health MarketScan® healthcare claims databases: 1) 2009–2015 Commercial Claims and Encounters Database and 2) 2009–2015 Multi-State Medicaid database (Truven Health MarketScan Databases, IBM Watson Health, Ann Arbor, MI)[12, 13]. The commercial databases include data for approximately 30–40 million employees and their beneficiaries each year from all US states covered by employer sponsored insurance. The Medicaid databases include data for approximately 6–13 million beneficiaries from 8–12 unidentified states. Both commercial and Medicaid databases include information on enrollment, inpatient and outpatient services, and outpatient pharmaceutical claims data for a subset of enrollees in the Commercial databases, including information on age and sex, clinical characteristics, medical procedures and pharmaceutical treatment. Enrollees are assigned a de-identified unique number which allows linkage of claims over time. The commercial databases contain a family identifier that allows linkage of family members enrolled together under a single subscriber policy; we used this variable to identify mothers of commercially-insured infants in order to calculate maternal age. Only the Medicaid databases include information on race/ethnicity. This study of de-identified data was determined not to require institutional review board review.

Case Definitions

Our study cohort was created by first identifying infants with congenital CMV disease who met our study criteria. We then pulled all their claims with a CMV-associated condition, hearing loss, brain imaging procedures, and valganciclovir treatment.

For this study, criteria for inclusion were infants who were continuously enrolled for at least 45 days after their first claim with an International Classification of Disease, 9th or 10th Revisions, Clinical Modification (ICD-9-CM or ICD-10-CM) or diagnosis-related group code for live birth and for whom outpatient pharmaceutical claims data were available. Infants who died in the hospital before 45 days were excluded from the analysis. For infants enrolled in Medicaid, we included those with known basis of Medicaid eligibility, which included children in low-income families, children born to mothers on Medicaid (these children are automatically covered for their first year of life), and disabled individuals who qualify for the Supplemental Security Income program; states have flexibility in their Medicaid programs to include additional groups[14].

The diagnosis of congenital CMV infection must be confirmed by laboratory testing within 2 to 3 weeks of birth, and laboratory results were not captured by claims databases. We identified infants diagnosed with congenital CMV disease by the presence of an ICD-9-CM or ICD-10-CM code of congenital CMV infection or CMV disease within 45 days. We used 45 days because of potential delays in submission of a claim. Among infants diagnosed with congenital CMV disease, we assessed the frequency of CMV-associated conditions, hearing loss, brain imaging procedures, and valganciclovir treatment. Using ICD-9-CM or ICD-10-CM codes, we also assessed the following CMV-associated conditions within 45 days: jaundice, petechiae, hepatomegaly, splenomegaly, microcephaly, thrombocytopenia,

chorioretinitis, and brain abnormalities (Appendix Table 1). We defined hearing loss by the presence of either ≥3 medical encounters with an ICD-9-CM or ICD-10-CM code of hearing loss or ≥1 claim with a Current Procedural Terminology (CPT) code of hearing aid or cochlear implant within 180 days. Brain imaging procedures included head computed tomography (CT) scans or magnetic resonance imaging (MRI) using CPT codes recorded within 45 days. We assessed valganciclovir treatment by the presence of any valganciclovir claim within 180 days using codes listed in the National Drug Code Directory (Appendix Table 1).

Analysis

We performed all analyses using SAS version 9.3 (SAS Institute, Cary, North Carolina). We assessed trends in valganciclovir claims over time using the Cochrane Armitage trend test. We conducted univariate analyses to compare selected characteristics between infants diagnosed with congenital CMV infection among the commercially-insured and Medicaid-insured infants, and to assess whether presence of any CMV-associated conditions or hearing loss was associated with valganciclovir treatment using Pearson chi square or Fisher's exact test. We considered results with a p-value <0.05 as statistically significant.

RESULTS

We identified 1,163,112 commercially-insured infants and 1,357,945 Medicaid-insured infants, among whom 257 (2.5/10,000 infants) and 445 (3.3/10,000 infants) were diagnosed with congenital CMV disease, respectively. The proportion diagnosed with congenital CMV disease significantly increased during the study period among commercially-insured infants (p=0.0155 for test of trend; regression slope=2.03), but not among Medicaid-insured infants (p=0.3755 for test of trend; regression slope = −3.53) [Figure 1A]. Demographic characteristics of all infants who met the study criteria, infants diagnosed with congenital CMV disease, and those with congenital CMV disease and valganciclovir treatment are shown in Table 1. The median maternal age was 32 years (range, 20–45 years) for commercially-insured infants with congenital CMV disease; this information was not available for the Medicaid-insured infants. Five (0.7%) infants with congenital CMV disease died in hospitals within 142 days—two commercially-insured and three Medicaid-insured infants.

Many of the infants with congenital CMV disease had ≥1 CMV-associated condition, 135 (53%) in the commercially-insured group and 282 (63%) in the Medicaid-insured group [Table 2]. Among all 257 and 445 commercially-insured and Medicaid-insured infants, respectively, diagnosed with congenital CMV disease, 30 (12%) and 32 (7%) had hearing loss and 51 (20%) and 99 (22%) had a neurological abnormality (microcephaly, chorioretinitis and/or brain abnormality). Among a subset of infants with congenital CMV disease enrolled continuously for the first 180 days of life, 25 out of 203 (12%) commercially-insured and 28 out of 294 (10%) Medicaid-insured infants had hearing loss. The proportion of infants with congenital CMV disease who had undergone CT declined significantly during 2009–2015, from 17% to 7% among commercially-insured and from 21% to 8% among Medicaid-insured infants. Although the proportion of those who had

undergone MRI increased from 6% to 11% among commercially-insured and from 9% to 16% among Medicaid-insured infants, this increase was not statistically significant. Among a subset of infants with congenital CMV disease who had undergone brain imaging, 52% (28/54) commercially-insured and 35% (32/91) Medicaid-insured infants had brain abnormalities.

Overall, among infants with congenital CMV disease, 41 (16%) commercially-insured and 78 (18%) Medicaid-insured infants had valganciclovir treatment. The proportion of infants with congenital CMV disease who had valganciclovir treatment increased significantly during 2009–2015, from 0% (0/35) to 29% (8/28) among commercially-insured infants, and from 4% (3/67) to 37% (28/76) among Medicaid-insured infants ($p<0.0001$) [Figure 1B]. The median age at the first valganciclovir treatment claim was 24 days (range, 0–131) among commercially-insured infants, and 30 days (range, 5–163) among Medicaid-insured infants; 76% (31/41) and 73% (57/78), respectively, had their first valganciclovir treatment claim within 45 days of life. The median interval between the first valganciclovir claim and last valganciclovir claim for 119 infants with congenital CMV disease and valganciclovir treatment in this study was 61 days (median of 98 days for commercially-insured and 44 days for Medicaid-insured infants), with the interval being < 6 weeks for 43%, 6 weeks-6 months for 53%, and >6 months for 4%.

The majority of infants with congenital CMV disease who had valganciclovir treatment had ≥1 CMV-associated condition and/or hearing loss (90% and 87% among commercially and Medicaid-insured infants, respectively). Among infants with congenital CMV disease who had valganciclovir treatment, 2 (5%) commercially-insured and 3 (4%) Medicaid-insured infants had hearing loss without any other CMV-associated condition. Valganciclovir treatment among infants with congenital CMV disease was significantly associated with petechiae, splenomegaly, microcephaly, thrombocytopenia, brain abnormalities, any neurologic abnormality, ≥2 CMV-associated conditions, and hearing loss, in both commercially- and Medicaid-insured infants; with chorioretinitis among commercially-insured infants only; and with hepatomegaly among Medicaid-insured infants only [Table 3]. When we restricted to infants with only 1 CMV-associated condition, valganciclovir treatment was significantly associated with infants with microcephaly alone among commercially insured infants with congenital CMV disease, and with jaundice alone or brain abnormalities alone among Medicaid insured infants.

DISCUSSION

In 2012, the AAP recommended that treatment with valganciclovir be considered for infants with symptomatic congenital CMV disease with CNS involvement[10]. Using a large national healthcare claims database, we found that approximately 20% of infants identified with congenital CMV disease in the United States were treated with valganciclovir, with an increasing trend during 2009–2015. We could not assess factors that were associated with increasing trends in valganciclovir treatment among infants with congenital CMV disease. However, we can speculate that these increases may be due to increased use of valganciclovir in place of IV ganciclovir because valganciclovir can be administered in an outpatient setting, and rates of neutropenia appear to be lower than with IV ganciclovir[9]. The

rise in valganciclovir may also be due in part to increased awareness among physicians and insurance coverage of antiviral treatment likely contributed to these increasing trends. The publication of studies on the use of valganciclovir to treat neonates with symptomatic congenital CMV disease starting in 2008, and AAP's recommendation on antiviral treatment may have helped to increase awareness among physicians[8–11].

Using convenience samples of commercially- and Medicaid-insured infants, we found the prevalence of congenital CMV disease was 2 to 3 per 10,000. The prevalence of congenital CMV disease was higher among infants with Medicaid insurance (3.3 per 10,000) compared to commercially-insured infants (2.5 per 10,000), which likely reflects a higher proportion of Medicaid infants with underlying conditions and risk factors associated with congenital CMV infection, such as non-White race, or other maternal characteristics, such as age or socioeconomic status, that could not be measured[15]. A study that looked at RSV hospitalizations among commercially and Medicaid insured infants also found higher rates of hospitalizations and more severe cases among Medicaid-insured infants[16]. Data from this study and others suggest that not all infants with symptomatic congenital CMV disease are diagnosed or captured using administrative healthcare claims[17, 18]. We observed a prevalence of symptomatic congenital CMV disease that was between one-half and one-third of the expected 5.0–7.5 per 10,000 prevalence in the United States[2]. One study by Diener et al.[19] found that the proportion of diagnosed symptomatic congenital CMV cases may be as high as 30%, though other studies have found this proportion to be much lower, with <10% of symptomatic cases diagnosed[17, 18, 20].

Studies evaluating the sensitivity, specificity, and accuracy of administrative healthcare claims to capture certain conditions among infants have found that specificity and sensitivity can vary greatly by condition and by whether the claim was identified from an inpatient or outpatient setting[21–26]. Because our study relies on use of administrative data based on convenience samples of infants with commercial or Medicaid insurance, our study had a number of limitations. Our data may not be generalizable to all US infants, and Medicaid data are from a select number of states. There may have been errors in the diagnostic and procedural coding for congenital CMV disease, CMV-associated conditions, brain abnormalities, and hearing loss. It is possible that infants with congenital CMV disease may have had CMV-associated conditions, such as intrauterine growth restriction or abnormal brain imaging findings that were not included in our study or captured in the claims. Laboratory test results and medical records were unavailable to confirm the diagnosis of congenital CMV disease. We also may have missed deaths and hearing loss that occurred after the study observation time.

It is possible that we did not accurately capture data within the first 45 days because we did not have birth date and therefore had to approximate the birth date using the first claim with a live birth code. There may also be a delay in the enrollment of a newborn in a health plan. As a result, we may have missed newborns with a CMV diagnosis or valganciclovir treatment using the 45-day continuous enrollment criteria. Using another enrollment criteria (infants with a newborn inpatient claim and enrolled at 45 days of life), we found no changes in the trends of CMV diagnosis or valganciclovir treatment among commercial- or Medicaid-insured infants. Lastly, we did not have access to inpatient antiviral treatment, so

we were unable to evaluate trends in IV ganciclovir use and complete history of antiviral treatment over time.

Many of the infants with congenital CMV disease in this study had a CMV-associated condition and/or hearing loss. Most infants identified with congenital CMV disease who also had valganciclovir treatment had CMV-associated conditions, among which petechiae, splenomegaly, microcephaly, thrombocytopenia, hearing loss, and brain abnormalities were significantly associated with valganciclovir treatment. We found that the majority of congenital CMV cases were treated within the first 45 days: 76% among the commercially-insured and 73% among the Medicaid-insured infants. These findings suggest that current management of a majority of infants with congenital CMV disease is in line with the recommendations of the American Academy of Pediatrics, which consists of antiviral treatment for management of symptomatic congenital CMV disease for infants who are able to start treatment within the first month[11]. In a minority of treated infants, underreporting of CMV-associated conditions or treatment of asymptomatic infants with hearing loss only are possible. There has been limited clinical experience of use of antivirals in infants with asymptomatic congenital CMV infection with isolated hearing loss[27–29]. However, this has not been systematically evaluated in a randomized controlled trial or study, thus, there is no evidence to support treatment of infants with asymptomatic congenital CMV infection.

Symptomatic congenital CMV disease frequently involves the central nervous system and results in neurodevelopmental sequelae[1, 4, 30–32]. Neuroimaging is useful to inform prognosis and guide clinical management of infants with congenital CMV disease[33]. Infants with congenital CMV disease and brain abnormalities suggesting tissue destruction (i.e. intracranial calcifications, white matter lucency) or dysplastic growth (i.e. lissencephaly, pachygyria) are at increased risk of intellectual disability and SNHL[34]. In this study, we found that approximately 20% of infants with congenital CMV disease had CT or MRI performed within the first 45 days, among whom 41% had a diagnosis of at least one brain abnormality. We also found a decreasing trend over time in use of head CT for neuroimaging evaluation of infants with congenital CMV disease, among both the commercially- and Medicaid-insured infants, and an increasing, albeit non-significant, trend in MRI use. These findings are consistent with more recent recommendations for neuroimaging evaluation using MRI or ultrasound because CT scans can lead to high exposure to radiation[3533, 36].

In the absence of surveillance or newborn screening for congenital CMV infection, administrative data can be useful to assess national trends in diagnosis and management of infants with symptomatic congenital CMV disease. Further studies are needed to assess the accuracy, sensitivity and specificity of using administrative claims data for identifying infants with congenital CMV infection and evaluating factors associated with increasing trends in valganciclovir use.

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Abbreviations

AAP	American Academy of Pediatrics
CMV	Cytomegalovirus
CPT	Current Procedural Terminology
CT	computed tomography
ICD-10-CM	International Classification of Disease, 10th Revision, Clinical Modification
ICD-9-CM	International Classification of Disease, 9th Revision, Clinical Modification
IV	intravenous
MRI	magnetic resonance imaging
SNHL	sensorineural hearing loss

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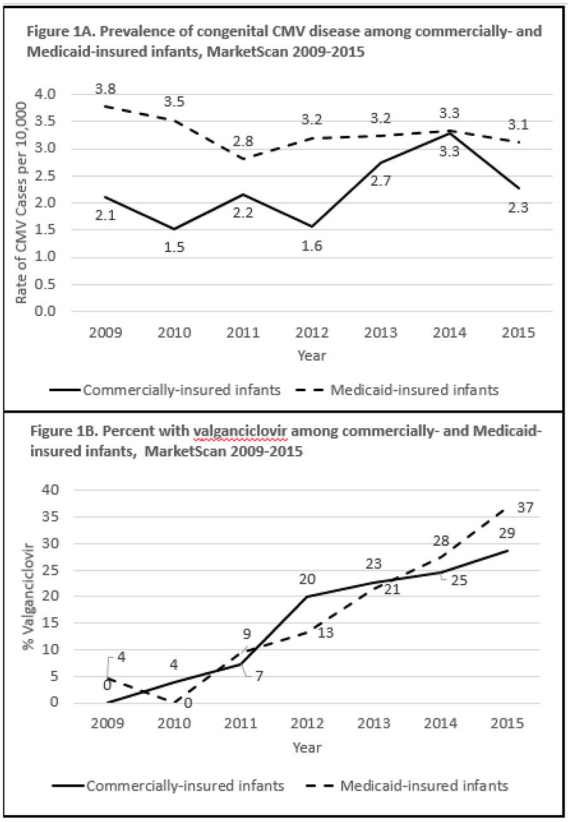

Figure 1.

Rate of congenital CMV disease and proportion with valganciclovir among infants with congenital CMV disease, MarketScan Commercial Claims and Encounters and Medicaid Databases 2009–2015

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Table 1

Demographic characteristics of all infants, infants with congenital CMV disease, and infants with congenital CMV disease and valganciclovir treatment, MarketScan Commercial Claims and Encounters and Medicaid Databases, 2009–2015

	Commercially-insured Infants					
Variable	**All Infants (N=1,163,112)**		**Infants with congenital CMV disease (N=257)**		**Infants with congenital CMV disease and valganciclovir (N=41)**	
	#	**%**	**#**	**%**	**#**	**%**
Sex						
Male	600,748	52%	132	51%	15	37%
Female	562,364	48%	125	49%	26	63%
Region						
Northeast	210,326	18%	39	15%	6	15%
North Central	332,796	29%	56	22%	12	29%
South	428,378	37%	124	48%	12	29%
West	177,915	15%	32	12%	10	24%
Unknown	13,672	1%	6	2%	1	2%
Maternal Age (years)[a]						
15–19	3,289	0.3%	0	0%	0	0%
20–29	368,127	37%	71	32%	13	36%
30–39	584,913	59%	137	61%	21	58%
40–49	43,212	4%	15	7%	2	6%
All, 15–49	999,541	100%	223	100%	36	100%
	Medicaid-insured Infants					
Variable	**All infants (N=1,357,945)**		**Infants with congenital CMV disease (N=445)**		**Infants with congenital CMV disease and valganciclovir (N=78)**	
	#	**%**	**#**	**%**	**#**	**%**
Sex						
Male	693,241	51%	220	49%	43	55%
Female	664,704	49%	225	51%	35	45%
Race						
White	606,229	45%	136	31%	24	31%

Variable	All Infants (N=1,163,112)		Commercially-insured Infants: Infants with congenital CMV disease (N=257)		Commercially-insured Infants: Infants with congenital CMV disease and valganciclovir (N=41)	
	#	%	#	%	#	%
Black	412,226	30%	180	40%	18	23%
Hispanic	109,712	8%	18	4%	4	5%
Other	229,778	17%	111	25%	32	41%

[a]The commercial databases contain a family identifier that allows linkage of family members enrolled together under a single subscriber policy; we used this variable to identify mothers of commercially-insured infants in order to calculate maternal age. To identify moms of enrolled infants, we identified another enrolled family member who was a women aged 15 to 49 years with a claim for delivery from inpatient admissions (Major Diagnostic Category 14 or 15) that occurred within −90 to 10 days of first newborn code.

Table 2

Characteristics of infants with a CMV diagnosis, by insurance type, MarketScan Commercial Claims and Encounters and Medicaid Databases 2009–2015

Variable	Commercially-insured Infants with congenital CMV disease (N=257)		Medicaid-insured Infants with congenital CMV disease (N=445)		
	#	%	#	%	*p*-value
Sex					
Male	132	51%	220	49%	0.6389
Female	125	49%	225	51%	
Type of CMV Diagnostic Code[a]					
Congenital CMV	194	75%	360	81%	0.1025
CMV Disease	117	46%	196	44%	0.7526
CMV-associated conditions in first 45 days[a]					
Jaundice	75	29%	171	38%	**0.0139**
Petechiae	9	4%	22	5%	0.4479
Hepatomegaly	8	3%	20	4%	0.4279
Splenomegaly	6	2%	11	2%	1.0000
Microcephaly	16	6%	42	9%	0.1556
Thrombocytopenia	60	23%	137	31%	**0.0366**
Chorioretinitis	9	4%	17	4%	1.0000
Brain abnormalities	43	17%	59	13%	0.2222
Neurological abnormalitiy[c]	51	20%	99	22%	0.4543
Any of the above conditions	135	53%	282	63%	**0.0053**
Number of conditions					
0	122	47%	163	37%	**0.0053**
1	81	32%	154	35%	0.4550
≥2	54	21%	128	29%	**0.0255**
Hearing Loss					
Hearing Loss in first 180 days (either ≥3 hearing loss dx codes, or ≥1 hearing aid code)	30	12%	32	7%	0.0529
Died[b]	2	1%	3	1%	1.0000
Brain Imaging[a]					

Variable	Commercially-insured Infants with congenital CMV disease (N=257)		Medicaid-insured Infants with congenital CMV disease (N=445)		
	#	%	#	%	*p*-value
Any Imaging	147	57%	241	54%	0.4783
Ultrasound	127	49%	212	48%	0.6952
Computer tomography (CT)	23	9%	49	11%	0.4394
Magnetic Resonance Imaging (MRI)	36	14%	52	12%	0.4079
Valganciclovir					
No	216	84%	367	82%	0.6031
Yes	41	16%	78	18%	

[a] Categories are not mutually exclusive.

[b] Among commercially-insured infants with congenital CMV disease, there were 2 deaths; the interval between first live birth code and death was 98 and 142 days. Among Medicaid-insured infants with congenital CMV disease, there were 3 deaths; the interval between first live birth code and death was 52–100 days. All 5 deaths had CMV-associated conditions.

[c] Neurologic abnormalities included infants with microcephaly, chorioretinitis, and/or brain abnormalities.

Table 3

Factors associated with valganciclovir use among infants with congenital CMV disease, MarketScan Commercial Claims and Encounters and Medicaid Databases 2009–2015

Variable	Commercially-insured Infants					Medicaid-insured infants				
	Congenital CMV disease and NO valganciclovir claim (N=216)		Congenital CMV disease and valganciclovir claim (N=41)		*p*-value	Congenital CMV disease and NO valganciclovir claim (N=367)		Congenital CMV disease and valganciclovir claim (N=78)		*p*-value
	#	%	#	%		#	%	#	%	
CMV-associated conditions in first 45 days[a]										
Jaundice	60	28%	15	37%	0.2651	136	37%	35	45%	0.2025
Petechiae	5	2%	4	10%	**0.0387**	14	4%	8	10%	**0.0374**
Hepatomegaly	7	3%	1	2%	1.0000	12	3%	8	10%	**0.0131**
Splenomegaly	2	1%	4	10%	**0.0067**	5	1%	6	8%	**0.0054**
Microcephaly	5	2%	11	27%	**<0.0001**	28	8%	14	18%	**0.0091**
Thrombocytopenia	42	19%	18	44%	**0.0020**	91	25%	46	59%	**<0.0001**
Chorioretinitis	5	2%	4	10%	**0.0387**	11	3%	6	8%	0.0939
Brain abnormalities	27	13%	16	39%	**0.0001**	41	11%	18	23%	**0.0090**
Neurologic abnormalities[b]	31	14%	20	49%	**<0.0001**	64	17%	35	45%	**<0.0001**
Any of the above conditions	100	46%	35	85%	**<0.0001**	217	59%	65	83%	**<0.0001**
Number of conditions					**<0.0001**					
0	116	54%	6	15%	**<0.0001**	150	41%	13	17%	**<0.0001**
1	68	31%	13	32%	1.0000	133	36%	21	27%	0.1490
≥2	32	15%	22	54%	**<0.0001**	84	23%	44	56%	**<0.0001**
Hearing Loss										
Hearing Loss in first 180 days (either ≥3 hearing loss dx codes, or ≥1 hearing aid code)	19	9%	11	27%	**0.0026**	13	4%	19	24%	**<0.0001**

[a] Categories are not mutually exclusive.

[b] Neurologic abnormalities included infants with microcephaly, chorioretinitis, and/or brain abnormalities.

Appendix Table 1

List of Diagnostic, Procedural, and Drug Codes

Code(s)	Code Description
Newborn Codes	
ICD-9-CM V30–31, V33–4, V36, V37, V39; ICD-10 CM Z38.xx	Live birth
DRG 791–795	Prematurity with and without Major Problems, Full Term Neonate with Major Problems, Neonate with Other Significant Problems, Normal Newborn
Congenital cytomegalovirus (CMV), CMV Disease, and CMV-Associated Conditions	
ICD-9-CM 771.1; ICD-10 CM P35.1	Congenital CMV Infection
ICD-9-CM 078.5; ICD-10-CM B25.x	CMV Disease
ICD-9-CM 774; ICD-10-CM P58.x or P59.x	Jaundice
ICD-9-CM 772.6, 782.7; ICD-10-CM P54.5;	Petechiae
ICD-9-CM 751.69, 789.1; ICD-10-CM Q44.7, R16.0, R16.2, B25.1	Hepatomegaly
ICD-9-CM 759.0, 789.2; ICD-10-CM Q89.09, R16.1, R16.2	Splenomegaly
ICD-9-CM 742.1; ICD-10-CM Q02	Microcephaly
ICD-9-CM 776.1, 776.2, 287.3–287.5; ICD-10-CM P60, P61.0, D69.4x-D69.6x	Thrombocytopenia
ICD-9-CM 363.0–3; ICD-10-CM H30.0x, H30.1x, H30.89x, H30.9x, H31.00x	Chorioretinitis
ICD-9-CM 348.89, 742.2–742.4, 793.0; ICD-10-CM G91.xx, G93.89, G93.9, Q03.xx, Q04.xx, R90.82	Brain abnormalities
Hearing Loss (Diagnostic codes)	
ICD-9-CM 389.1x-389.9; ICD-10-CM H90.3x-H90.8x, H91.x	Hearing loss
Hearing Aid or Cochlear Implant Codes (Procedural codes):	
CPT 92590–92595; HCPCS V5010, V5011, V5014, V5020, V5060, V5090, V5140, V5160, V5241, V5247, V5253, V5257, V5261, V5264, V5275, V5298; ICD-9 v3 V53.2; ICD-10 Z46.1	Hearing aid
CPT 69710, 69930, 92510, 92601, 92602; HCPCS L8614	Cochlear Implant
Brain imaging (Procedural codes):	
CPT 70450, 70460, 70470, 70480, 70481, 70482	Computed tomography (CT)
CPT 70551–3	Magnetic Resonance Imaging (MRI)
Antiviral Treatment (Drug codes):	
NDC 00004003822, 00004003909 00603633020, 54569610100 55111076260,	Valganciclovir Hydrochloride
68084096525, 00591257920, 31722083260, 42291087560, 50268078711, 50268078712, 65862075360, 68084096595	

Abbreviations: ICD-9-CM=International Classification of Diseases-9th revision, ICD-10-CM = International Classification of Diseases-10th revision, Clinical Modification; DRG=Diagnoses Related Group; HCPCS= Healthcare Common Procedure Coding System; CPT= Current Procedural Terminology (CPT) codes; ICD-9 v3 Procedural Codes; NDC=National Drug Code