Incidence Trends, Risk Factors, Mortality and Healthcare Utilization in Congenital Syphilis-related Hospitalizations in the United States

A Nationwide Population Analysis

Krishna Kishore Umapathi, MD, Aravind Thavamani, MD, and Kobkul Chotikanatis, MD

Background : Congenital syphilis (CS) is a devastating yet preventable disease affecting the fetus. Recent increase in cases of CS in the United States has been reported by Centers for Disease Control and Prevention. There is a lack of data on hospitalization trends and healthcare utilization related to CS. We sought to describe CS hospitalization trends, morbidity and mortality during 2009 through 2016 and related healthcare expenditure.

Methods: National inpatient level data collected from Kid's Inpatient Database and National Inpatient Sample databases from 2009 to 2016 were analyzed. CS hospitalizations were identified using International Classification of Diseases codes in age less than 1 year. Related demographics, risk factors and outcomes were calculated. Infant mortality related to CS were calculated per number of hospitalizations.

Results: From 2009 to 2016, there were a total of 5912 CS-related hospitalizations. The overall trends in hospitalizations related to CS was up trending since 2009. African American ethnicity, public insurance/uninsured, low socioeconomic status, geographic location (South and West hospital regions), prematurity and low birth weight were significantly associated with CS and remained as independent risk factors. The mean length of stay (12.38 ± 0.10 d vs. 3.42 ± 0.1 d) and mean hospitalization charges were significantly higher in CS ($P < 0.001$) as compared with other hospitalized infants without CS. The total inflation-adjusted hospitalization charges have more than doubled over the years ($120,665,203 in 2016 vs. $54,290,310 in 2009). The rate of in-hospital deaths in CS hospitalization was 0.54% (32 deaths among 5912 hospitalizations).

Conclusions: The incidence of CS hospitalization has been increasing since 2009. CS contributes to a significant healthcare utilization burden; its prevention can save a large amount of healthcare-related expenditure.

Key Words: congenital syphilis, infant mortality, prenatal care, health care utilization

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Congenital syphilis (CS), caused by Treponema pallidum is transmitted from an infected mother via the transplacental route at any time during pregnancy, or at delivery when the newborn comes in contact with maternal lesions.[1] If the mother is not diagnosed, is diagnosed but not treated or is treated late in pregnancy, there is a high chance of CS in the offspring.[2,3] CS is a devastating condition with a very high morbidity and mortality including miscarriage, low birth weight (LBW), prematurity, stillbirth, neurologic sequelae and death in newborns. Still, it is a completely preventable condition and the disease burden could be significantly reduced by prompt screening of infected mothers and adequate treatment with penicillin.[4] Analyses of national case report data from 1992 to 1998 and from 1999 to 2013 done by Gust et al[5] and Su et al[6], respectively, showed declines in both overall cases of CS and death among CS with no significant trends noticed in the proportion of CS cases that died.

However, recently, Centers for Disease Control and Prevention (CDC) has noted an alarming rise in the number of CS cases that have been reported in the last 5 years. In 2017, the total case count of reported syphilis in all stages was the highest recorded in the last 2 decades.[7] No study on CS so far has reported data related to hospitalizations and its healthcare utilization. We report incidence of CS hospitalization over the last 8 years, risk factors and mortality associated with CS hospitalizations and healthcare utilization from a nationwide inpatient population-based database from 2009 to 2016.

MATERIALS AND METHODS

We analyzed the data from Agency for Healthcare Research and Quality sponsored Kids' Inpatient Database (KID) and Nationwide Inpatient Sample (NIS). The KID yields national estimates of hospital inpatient stays for patients younger than 21 years of age.[8] The NIS contains data on all hospital inpatient stays of all ages and from all the states participating in the Healthcare Cost and Utilization Project (HCUP).[9,10] Each year of the NIS includes over 7 million inpatient stays. Each sampled discharge record includes information on patient demographics, diagnosis and procedure codes and hospital characteristics. Our study received institutional review board approval from the Metro Health Medical Center and was deemed exempt from participation consent. KID databases are released almost every 3 years, and for this study, we analyzed 2009, 2012 and 2016 KID databases for CS-related hospitalizations. NIS databases are released annually, and since we wanted to measure the incident trends of CS-related hospitalizations each year, we also included data from NIS database from the years 2010, 2011, 2013, 2014 and 2015. All NIS and KIDS database employed International Classification of Diseases, 9th revision (ICD-9) codes for diagnoses up until the end of third-quarter of 2015 and beginning the last quarter of 2015 the coding was done based on International Classification of Diseases, 10th revision (ICD-10) codes. We included all patients who were less than 1 year of age and had an indicator for in-hospital birth. The CS group included patients with the following ICD codes (ICD-9 Code—"090.*", ICD-10 Code—"A50.*") mentioned in any of the first 15 diagnosis columns pertinent to that particular hospitalization. The remaining population in the same group who did not have a diagnosis of CS served as controls for comparison. For analysis, we divided the insurance into 3 categories: (1) Public—comprising of Medicaid and Medicare, (2) Private and (3) Self pay/

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Departments of Pediatrics and Pediatric Infectious Diseases at Metro Health Medical Center – Case Western Reserve University, Cleveland, Ohio.
Both Krishna Kishore Umapathi and Aravind Thavamani contributed equally to the writing of this manuscript and are considered first authors.
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Address for correspondence: Krishna Kishore Umapathi, MD, Department of Pediatrics, Metro Health Medical Center – Case Western Reserve University, 2500 Metro Health Drive, Cleveland, OH 44129. E-mail: krishnakishoreumapathi@gmail.com.

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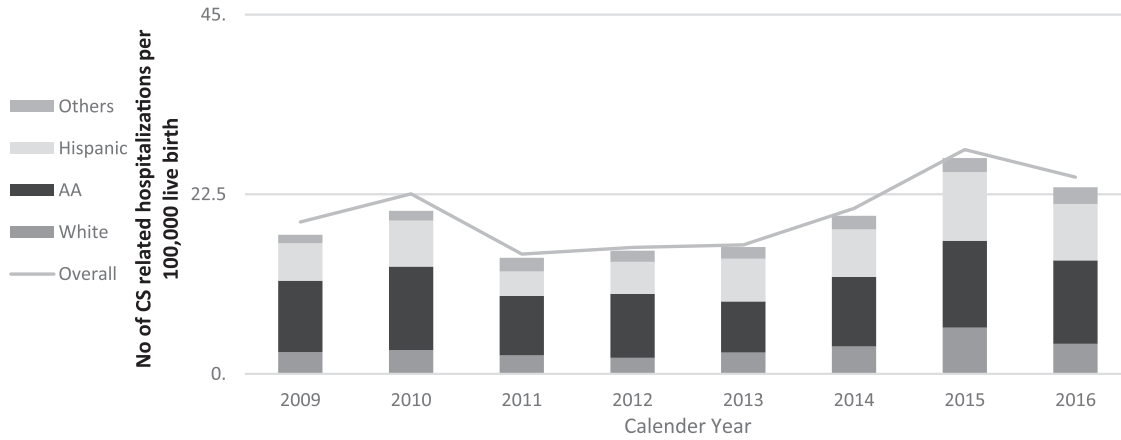

FIGURE 1. Number of hospitalizations of infants with ICD-9/ICD-10 diagnosis of congenital syphilis per 100,000 live births. AA, African American.

Uninsured—consists of self-pay, uninsured, no charge and others. For analysis, we divided birthweight into 4 categories: (1) less than 750 g, (2) 750–1499 g, (3) 1500–2500 g and (4) Non-LBW—above 2500 g. Prematurity was divided into (1) less than 29 weeks of gestation, (2) 29 weeks to 32 completed weeks of gestation, (3) 33 weeks to 36 completed weeks of gestation and (4) term (37 weeks of gestation and above). Hospitalization charges indicate the total expenditure reported for each discharge record (does not include professional fees). Total charges were missing in less than 5% of discharges. All charges were converted to 2016 US dollars using the medical consumer price index to adjust for inflation.[11] As per the HCUP publication guidelines, any variable in a category representing a patient count less than 10 should not be published to protect patient confidentiality and are not represented in this article. HCUP databases are publicly available deidentified national datasets and thus considered exempt from institutional review board.

STATISTICAL ANALYSIS

We used the HCUP weighting method to generate national estimates of all reported characteristics. All analyses were weighted using discharge weights provided by the KID and NIS database and national estimates were calculated. We report the frequency of CS as the number of estimated CS hospitalizations per 100,000 hospital admissions. Continuous data are reported as mean and SE. Categorical variables are reported as frequencies and percentages. Mann-Whitney *U* test was used for nonparametric data, and Pearson χ^2 test was used to compare categorical variables. Multiple logistic regression analysis was used to calculate adjusted odds ratio (aOR) and confidence intervals for various factors associated with CS hospitalizations. Linear by linear association was used to analyze the trend of hospital charges and length of stay (LOS) related to CS hospitalizations. For all statistical analysis, a P value of <0.05 or if confidence interval did not include 1.00, was considered significant. All statistical procedures were performed using SPSS version 24.0 (IBM Corporation, Armonk, NY).

RESULTS

During the 7-year time period ranging from 2009 to 2016, there were a total of 5912 CS-related hospitalizations. The incidence of CS-related hospitalizations was at an all-time low during the year 2011, and since then, the incidence rates are showing an upward trend (Fig. 1). The highest proportions were seen in infants of African American ethnicity (47%) followed by Hispanic ethnicity (29%) ($P < 0.001$) (Table 1). There was no gender predilection in CS-related hospitalizations, male (51%) vs female (49%), $P = 0.93$. A higher number of CS-related hospitalizations was associated with public insurance/uninsured (88%) and low median household income (57.5%), both $P < 0.001$. The number of CS-related hospitalizations showed a significant association with geographic location with hospitals in the South (59%) reporting the highest number followed by West (21%), $P < 0.001$. The mean LOS (CS: 12.38 ± 0.10 d vs. controls: 3.42 ± 0.1 d) and hospitalization charges (CS: $58,502 ± 1475 vs. controls: $12,592 ± 12.97) were significantly higher in CS when compared with other hospitalizations in the same age group related to any diagnosis other than CS (both $P < 0.001$). The total inflation-adjusted hospitalization charges have more than doubled over the years ($120,665,203 in 2016 vs. $54,290,310 in 2009) (Fig. 2). The total number of deaths related to CS were 32 among 5912 hospitalizations. The rate of deaths among hospitalizations in CS was 0.54% excluding stillbirths. Infant characteristics that were associated with mortality were LBW and gestational age. Missing information: number of hospitalizations with missing gender information were <10,304 did not have ethnicity data, < 10 had no details on insurance status and 112 hospitalizations did not have information on median household income.

On multivariate analysis, insurance status (private vs. public aOR 0.24), hospital region (South vs. Northeast, aOR 2.21), ethnicity (Black vs. White, aOR 6.51), median household income (>45,000 vs. < 25,000, aOR 0.36), prematurity (<29 weeks vs. term, aOR 3.01) and LBW (1500–2500 g vs. >2500 g, aOR 1.53) remained independent risk factors associated with CS (Table 2).

DISCUSSION

Incidence Trends

This is the first study to report national estimates of trends in CS-related hospitalizations in the United States. Korenromp et al[12] reported a global decrease in CS from 2012 to 2016 despite a stable maternal prevalence. Similarly, based on CDC data, Su et al[6] reported a declining trend in the incidence of stillbirths, morbid and nonmorbid CS between 1999 and 2013. However, since then there has been a gradual increase in reported CS cases to the CDC every year (362 cases in 2013, 462 cases in 2014, 492 cases in 2015, 639 cases in 2016 and 918 cases in 2017).[7,13] The reason for this alarming rise in CS is an increase in syphilis infection in pregnant women in the last 5 years that have been temporally associated to an increase in syphilis rates among men who have sex with men coupled with increased

TABLE 1. Baseline Characteristics in Hospitalizations With Congenital Syphilis

Characteristics	Subgroup	Congenital Syphilis	Control	*P*
Gender (n)	Male	3019	15,099,971	0.93
	Female	2887	14,406,796	
Race (n)	White	924	13,656,637	<0.001
	African American	2618	3,756,833	
	Hispanic	1611	5,444,439	
	Others	455	3,304,490	
Insurance (n)	Public	4695	13,517,554	<0.001
	Private	692	13,864,217	
	Uninsured	518	2,101,276	
Hospital region (%)	Northeast	7.8	1,220,987	<0.001
	Midwest	12.2	1,592,507	
	South	58.9	2,901,630	
	West	21.1	1,796,386	
Median household income (n)	$1–24,999	3335	8,079,016	<0.001
	$25,000–34,999	1256	7,266,953	
	$35,000–44,999	808	7,282,884	
	45,000 or more	401	6,435,478	
LBW (n)	<750	8	93,809	<0.001
	750–1499	458	940,919	
	1500–2500	187	245,690	
Preterm (n)	<29 weeks	113	212,431	<0.001
	29–32 weeks	213	348,140	
	33–36 weeks	849	1,840,321	
LOS, d (mean ± SE)		12.38 ± 0.10	3.42 ± 0.1	<0.001
Charges, 2016 $ (mean ± SE)		58,502 ± 1475	12,592 ± 12.97	<0.001
Mortality, n (%)		32/5912 (0.54%)	87,394/29,432,927 (0.29%)	0.001

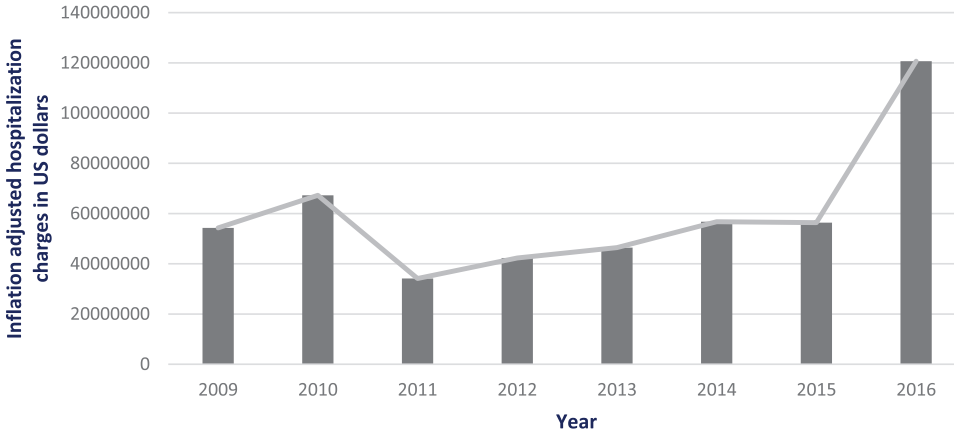

FIGURE 2. Trends in hospitalization charges (inflation-adjusted) of CS-related hospitalizations from 2009 to 2016.

drug use among women and heterosexual men.[14,15] Comparably, multiple studies conducted within other high-income nations including Spain, United Kingdom, Japan, have reported increases in syphilis cases among both women and men, possibly reflecting access to diagnosis and treatment services.[16–18]

Although in our study, the overall trend in CS-related hospitalizations was found to be increasing from 2009 to 2016, we noticed an initial increase in hospitalizations in 2009–2010 and then a gradual slowing for the next 2 years and then an uptrend again with the year 2016 seeing the highest reported hospitalizations. This is in stark contrast to the study which analyzed case trends from 1999 to 2013 and found a steady decline of CS cases that were reported to the CDC.[6] Another interesting finding was that the number of hospitalizations recorded in the databases was very high in comparison to the number of cases that were reported to the CDC.[7] This could be due to the fact that CDC has a passive data collecting system for sexually transmitted infections including CS and there is always a chance of CS being under reported due to the lack of active surveillance.

Baseline Characteristics

We included all hospitalizations associated with a primary diagnosis of CS in infants <12 months of age. Gender was not found to be an associated risk factor for acquiring CS. As shown in previous epidemiologic studies that reported ethnic variations in maternal and CS, we found that African American and Hispanic ethnicity were associated with higher number of CS-related hospitalizations.[6,19] Socioeconomic factors like low household income and public insurance status/uninsured status seem to be associated with an increased risk for CS.

We found a significantly higher number of CS-related hospitalizations in South and West regions in the United States. This is similar to CDC data which reported 70% of all cases that were reported were from 5 southern US states—Florida, California, Arizona, Texas and Louisiana. This geographic concentration of CS-hospitalizations might be secondary to the high number of immigrants in Florida, California and Texas and poor socioeconomic status in Louisiana.[20]

TABLE 2. Multiple Logistic Regression Demonstrating the Odds Ratio of Various Risk Factors of Congenital Syphilis-related Hospitalizations

Parameters	aOR (Lower CI–Upper CI)	*P*
Gender		
Male vs. female	1.09 (0.98–1.21)	0.11
Insurance		
Public	Reference	Reference
Private vs. public	0.24 (0.21–0.29)	<0.001
Uninsured vs. public	1.04 (0.87–1.24)	0.69
Hospital region		
Northeast	Reference	Reference
Midwest vs. Northeast	1.30 (1.02–1.66)	0.033
South vs. Northeast	2.21 (1.81–2.70)	<0.001
West vs. Northeast	2.01 (1.60–2.51)	<0.001
Race		
White	Reference	Reference
Black vs. White	6.51 (5.55–7.64)	<0.001
Hispanic vs. white	3.07 (2.58–3.65)	<0.001
Others vs. White	2.34 (1.87–2.92)	<0.001
Median household income		
<25,000	Reference	Reference
$25,000–34,999	0.66 (0.58–0.75)	<0.001
$35,000–44,999	0.60 (0.51–0.69)	<0.001
45,000 or more	0.36 (0.29–0.46)	<0.001
Birth weight		
Non-LBW	Reference	Reference
<750 vs. non-LBW	0.32 (0.13–0.80)	0.02
750–1499 vs. non-LBW	0.84 (0.63–1.11)	0.22
1500–2500 vs. non-LBW	1.53 (1.18–1.98)	0.001
Gestational age		
Term	Reference	Reference
<29 weeks vs. term	3.01 (1.95–4.64)	<0.001
29–32 vs. term	2.91 (2.12–4.0)	<0.001
33–36 vs. term	2.32 (1.92–2.81)	<0.001

CI indicates confidence interval.

Mortality and Outcome Measures

Su et al[6] reported 70 infant deaths related to CS in a 15-year time period between 1999 and 2013. Since then CDC has reported a significant increase in CS-related infant deaths including 13 infant deaths in the year 2017.[7] We report 32 infant deaths among the 5912 CS over the 7-year period (2009–2016). However, we could not trend the CS-related mortality every year due to insufficient numbers and the need to follow Data User Agreement-Agency for Healthcare Research and Quality of the databases to prevent patient identification.[21]

Hospital resource utilization trends as measured by LOS and hospital charges were significantly higher in CS group. The LOS remained fairly stable over the last 8 years for both CS and non-CS–related hospitalizations (Table 4). Despite no significant change in LOS, we report a significant increase in hospital expenditure for CS-related hospitalizations (Table 3). We assume this is related to the comorbidities that have been known to be associated with CS like prematurity, LBW, other central nervous system complications including meningitis and intensive care costs.[7]

STRENGTHS

This study has several strengths. First, it has a large sample size of hospitalized infants with ICD-9/10 codes for CS. Infants with CS need hospitalization for treatment with intravenous penicillin. This sample likely includes CS cases not reported to local/state health departments nor CDC.

Secondly, this is the first study to report various parameters collected from hospitalizations related to CS including incidence

TABLE 3. Mean Hospital Charges for All Hospitalizations With Congenital Syphilis Versus All Other Hospitalizations

Ospitalizations	2009	2010	2011	2012	2013	2014	2015	2016	*P* for Trend
CS-related hospitalizations									
Unweighted sample size	974	1053	669	740	790	950	800	1215	
Mean Hospitalization Charges, 2016 US $ (Range Limits)	56,156 (622–1,341,897)	63,509 (344–733,423)	51,527 (721–544,591)	58,066 (1004–1,486,768)	59,840 (1064–564,962)	61,415 (1323–757,289)	70,791 (2352–677,513)	100,674 (107–2,825,880)	<0.001
All other hospitalizations									
Unweighted sample size	4,599,735	4,471,109	4,261,468	4,269,244	4,226,598	4,246,805	7,109,580	4,251,487	
Mean Hospitalization Charges, 2016 US $ (Range Limits)	14,916 (100–1,499,997)	15,968 (100–1,497,616)	16,029 (100–4,994,014)	18,141 (100–4,981,665)	18,530 (100–4,969,916)	19,552 (101–4,999,975)	18,476 (100–4,964,157)	22,871 (101–6,948,132)	<0.001

TABLE 4. Trends in Mean Length of Stay of Congenital Syphilis-related Hospitalizations Versus Controls

Year	Mean LOS-CS	Mean LOS-Controls
2009	13.22 ± 0.53	3.76 ± 0.004
2010	12.98 ± 0.38	3.92 ± 0.004
2011	13.92 ± 0.68	3.74 ± 0.004
2012	12.67 ± 0.54	3.84 ± 0.005
2013	11.91 ± 0.35	3.82 ± 0.004
2014	12.03 ± 0.37	3.85 ± 0.005
2015	12.15 ± 0.44	3.70 ± 0.003
2016	13.07 ± 0.43	3.94 ± 0.004

trends and healthcare utilization of CS in the United States. Another important implication of the study is that the number of hospitalizations outnumber the number of cases reported to CDC (years 2013, 2014, 2015, 2016) which might represent missed opportunities and need for an active robust surveillance and reporting system.

LIMITATIONS

Although the KID and NIS database enjoy the advantages of having a number of strengths, our study does have limitations. First, it is a retrospective study and the use of retrospective data in our analysis comes with a certain degree of uncertainty due to the possibility of error in coding that should be carefully considered in interpreting our data. Second, our report lacks information on quality of health care including data about maternal risk factors that may have contributed to the development and progression of CS which include number of sexual partners, history of drug use or access and utilization of prenatal care. Third, although we report higher number of CS hospitalizations (as compared with CDC reported CS cases), multiple factors could have contributed to this (1) Under reporting: CDC is a passive data collective system where there is a high possibility for under reporting of cases, (2) Duplication: Our data include number of hospitalizations and may include readmissions and (3) CS is difficult to diagnose. Misdiagnosis of CS is common. Overtreatment and overdiagnosis occur. Providers may classify an infant as having CS without that infant meeting the CDC case definition. For example, despite having a mother with adequately treated syphilis during pregnancy, some providers may presumptively diagnose and treat infants for this infection. Fourth, we used hospital charges to estimate healthcare utilization costs, which may not be an actual reflection of hospital costs. In addition, there is a possibility of hospital billing protocols changing over time which could account for the reported increase in trends of hospitals charge for CS. Finally, mortality from CS could have been underreported due to the following reasons: (1) Stillbirths due to CS were not included, (2) Manual reporting errors by providers and within ICD coding databases and (3) The analysis was done based on discharge level diagnosis, and it is a known fact that at least some of syphilis-related morbidity and mortality will manifest several months or years later.[1]

CONCLUSIONS

There is a steady and exponential increase in CS hospitalizations in the United States. Race, socioeconomic factors and geographic location play a major role in influencing the incidence of CS in United States. Our study illustrates the racial and socioeconomic disparities of infants affected with CS. There is a high mortality associated with CS with LBW and prematurity are associated with a poor prognosis. CS contributes to a significant healthcare burden and its prevention can save a large amount of healthcare-related expenditure (estimated 345 million dollars spent from 2009 to 2016) in the United States. The rise in this tragic yet preventable disease is a major health concern and should be taken seriously and addressed accordingly. Syphilis screening and early treatment as part of routine antenatal care and treatment of sexual partners, can prevent CS in newborns and reduce the burden of this preventable adverse outcome. Active or multilevel surveillance can improve the burden estimation and help guide focused prevention efforts.

REFERENCES

1. American Academy of Pediatrics. Syphilis. In: Kimberlin DW, Brady MT, Jackson MA, et al, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases*. American Academy of Pediatrics; 2018:773–788.
2. Gomez GB, Kamb ML, Newman LM, et al. Untreated maternal syphilis and adverse outcomes of pregnancy: a systematic review and meta-analysis. *Bull World Health Organ*. 2013;91:217–226.
3. Ingraham NR Jr. The value of penicillin alone in the prevention and treatment of congenital syphilis. *Acta Derm Venereol Suppl (Stockh)*. 1950;31(suppl 24):60–87.
4. Alexander JM, Sheffield JS, Sanchez PJ, et al. Efficacy of treatment for syphilis in pregnancy. *Obstet Gynecol*. 1999;93:5–8.
5. Gust DA, Levine WC, St Louis ME, et al. Mortality associated with congenital syphilis in the United States, 1992–1998. *Pediatrics*. 2002;109:E79-9.
6. Su JR, Brooks LC, Davis DW, et al. Congenital syphilis: trends in mortality and morbidity in the United States, 1999 through 2013. *Am J Obstet Gynecol*. 2016;214:381.e1–e9.
7. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance 2017. Atlanta, GA: US Department of Health and Human Services; 2018. Available at: https://www.cdc.gov/std/stats17/toc.htm. Accessed January 20, 2019.
8. Healthcare Cost and Utilization Project (HCUP). HCUP Kids' Inpatient Database (KID). Rockville, MD: Agency for Healthcare Research and Quality; 2016. Available at: www.hcup-us.ahrq.gov/kidoverview.jsp. Accessed January 20, 2019.
9. Healthcare Cost and Utilization Project (HCUP). HCUP National Inpatient Sample (NIS). Rockville, MD: Agency for Healthcare Research and Quality; 2012. Available at: www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed January 20, 2019.
10. Healthcare Cost and Utilization Project (HCUP). HCUP Nationwide Inpatient Sample (NIS). Rockville, MD: Agency for Healthcare Research and Quality; 2011. Available at: www.hcup-us.ahrq.gov/nisoverview.jsp. Accessed January 20, 2019.
11. US Bureau of Labor Statistics. 2010 Consumer Price Index; 2010. Available at: http://www.bls.gov/cpi/. Accessed May 31, 2019.
12. Korenromp EL, Rowley J, Alonso M, et al. Global burden of maternal and congenital syphilis and associated adverse birth outcomes—estimates for 2016 and progress since 2012. *PLoS One*. 2019;14:e0211720.
13. Bowen V, Su J, Torrone E, et al. Increase in incidence of congenital syphilis - United States, 2012-2014. *MMWR Morb Mortal Wkly Rep*. 2015;64:1241–1245.
14. An Q, Wejnert C, Bernstein K, et al; NHBS Study Group. Syphilis screening and diagnosis among men who have sex with men, 2008–2014, 20 U.S. cities. *J Acquir Immune Defic Syndr*. 2017;75(suppl 3):S363–S369.
15. Kidd SE, Grey JA, Torrone EA, et al. Increased methamphetamine, injection drug, and heroin use among women and heterosexual men with primary and secondary syphilis - United States, 2013–2017. *MMWR Morb Mortal Wkly Rep*. 2019;68:144–148.
16. Simms I, Ward H. Congenital syphilis in the United Kingdom. *Sex Transm Infect*. 2006;82:1.
17. Rodríguez-Cerdeira MC, Silami VG. Actualización en sífilis congénita. *Rev Int Dermatol Dermocosmet Clin*. 2003;6:248–56.
18. Kamb ML, Taylor MM, Ishikawa N. Rapid increases in syphilis in reproductive-aged women in Japan: a warning for other countries? *Sex Transm Dis*. 2018;45:144–146.
19. Slutsker JS, Hennessy RR, Schillinger JA. Factors contributing to congenital syphilis cases - New York City, 2010-2016. *MMWR Morb Mortal Wkly Rep*. 2018;67:1088–1093.
20. The Lancet. Congenital syphilis in the USA. *Lancet*. 2018;392:1168.
21. Healthcare Cost and Utilization Project (HCUP). Nationwide Data Use Agreement. Rockville, MD: Agency for Healthcare Research and Quality; 2017. Available at: www.hcup-us.ahrq.gov/team/NationwideDUA.jsp. Accessed January 20, 2019.