The Cost of a Preventable Disease: Estimated U.S. National Medical Expenditures for Congenital Syphilis, 1990

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Others who contributed to the study are listed in the box on page 404.

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Synopsis

Reported cases of congenital syphilis have increased rapidly in recent years. The purpose of this study was to estimate first-year medical care expenditures among 1990 incident cases of infants diagnosed with congenital syphilis.

The authors used a synthetic estimation model to calculate expenditures for congenital syphilis as the number of treated cases multiplied by cost per case. The number of cases was derived from surveillance data adjusted for underreporting and presumptive (false-positive) treatment. Cost per case was based on expected hospital and physician charges applied to case treatment protocols appropriate to case severity.

Base-case estimated first-year medical expenditure for 1990 treated cases (N = 4,400) in 1990 was $12.5 million. In sensitivity analysis, estimates ranged from $6.2 million to $47 million.

Substantial reduction in congenital syphilis treatment costs could be achieved through targeted public health interventions consisting of prenatal maternal screening and contact tracing of males testing positive for syphilis. Physicians should be aggressive in presumptive treatment of newborns, since this usually prevents future disability but represents a small portion of total national expenditure for congenital syphilis. More precise data on severe cases resulting in long-term disability are needed to make reliable cost estimates.

CONGENITAL SYPHILIS—syphilis vertically transmitted to the fetus during pregnancy—emerged during the 1980s as a serious threat to the health of children. The recent increase in reported cases of congenital syphilis (CS) in the United States is due to both an increase in actual cases and to broadening of the surveillance definition of CS in 1988 (*1,2*).

Increased incidence of CS is due to several factors. These factors include the rise in cases of primary and secondary syphilis among women of childbearing age (*3*), maternal reinfection, and the failure to detect many cases of maternal syphilis because of poor prenatal care or failure to perform serological tests for syphilis. More than 80 percent of persons with CS cases in the late 1980s received either no prenatal care or suboptimal care, thereby thwarting opportunities for prevention (*4*).

The previous definition of CS was based upon Kaufman's criteria, which required symptoms and laboratory findings at birth and serologic results collected in subsequent followup visits (*5*). These criteria were inappropriate for surveillance because of technical complexity and confusion surrounding case reporting categories of "definite," "probable," and "possible" (*6*). Furthermore, they did not include stillbirth occurring to mothers with untreated syphilis even though as much as 20 percent of stillbirths were attributed to CS in some geographic areas.

The new CS case definition includes all live-born and stillborn infants of women with a history of

Additional Contributors

Hong Wen Zhao, MD, is with the Bureau of Maternal and Child Health, Ministry of Public Health, People's Republic of China.

Kenneth Bromberg, MD, Division of Pediatric Infectious Disease, Department of Pediatrics, SUNY Health Science Center at Brooklyn, NY, reviewed and validated model results based on clinical experience in New York City.

Barbara J. Stoll, MD, Division of Neonatology, Department of Pediatrics, Emory University School of Medicine, Atlanta, GA, offered advice in project design and development and reviewed the congenital syphilis (CS) disease severity classification designed for the study and the protocols for management of CS.

Roselyn Rice, PhD, Deputy Director, Division of Sexually Transmitted Diseases Laboratory Research, Centers for Disease Control and Prevention (CDC), Atlanta, GA, served as project officer and obtained access to CS case reporting system files maintained by CDC.

untreated or inadequately treated syphilis, regardless of neonatal symptoms or findings (*7*). New York City adopted this simplified definition in 1989 and was joined in 1990 by many of the States that usually have the largest numbers of reported CS cases. Most other States and reporting areas implemented the new criteria in 1991 (*8*).

Knowledge of expenditures attributable to treating CS relative to other communicable disease would be useful in setting priorities for public health prevention and treatment programs. While the Centers for Disease Control and Prevention (CDC), in cooperation with local public health authorities, has developed reporting systems to track the incidence of CS, there have been no studies to determine outlays for the treatment of CS. Our objective was to develop an initial estimate of national medical expenditures for infants with CS.

Methods

Approaches to determining expenditure for a disease include analysis of health insurance claims data and review of medical records. Most CS occurs among low-income persons lacking health insurance whose sources of clinical care are fragmented. Therefore, analysis of health insurance claims data or hospital billing records is likely to underestimate outlays. We used a synthetic estimation model to calculate the national direct medical cost of CS cases identified during 1990. In this approach, the number of cases of a disease is multiplied by the estimated average cost of care per case to yield the total cost of care. National medical costs for care of persons infected with the human immunodeficiency virus (HIV) have been estimated using this method (*9*). Our baseline for the number of infants who may have been treated for CS in 1990 was the 3,484 cases recorded in the CDC national syphilis surveillance system. The main tasks of our analysis were to estimate the cost per case and to adjust the number of CS cases as reported to CDC to allow for incomplete reporting.

Case classification. Presentation of CS varies according to disease severity and other factors. Cost of care and outcome of treatment may also vary as a function of case severity. The precision of a synthetic cost estimate can be improved by subdividing the total number of cases into categories differentiated by expected level of resource use. Instead of multiplying the total number of cases by an average cost per case, the number of cases in each category is multiplied by the estimated cost of care for persons in that category.

The effect of syphilis on the fetus depends on the developmental stage when infection takes place, the interval between infection and treatment, and the treatment modality. Untreated early infections may result in abortion, stillbirth, neonatal death, intrauterine growth retardation, or premature delivery (*10*). At least half of infected live-born infants have no signs of CS at birth (*11,12*). Clinical manifestations appearing within the first 2 years of life are termed early, and those occurring after this time are called late (*10*). Signs of early CS include condyloma lata, snuffles, syphilitic skin rash, hepatosplenomegaly, jaundice due to syphilitic hepatitis, pseudoparalysis, or edema. Stigmata of late CS include interstitial keratitis, nerve deafness, anterior bowing of shins, frontal bossing, mulberry molars, Hutchinson's teeth, saddle nose, rhagades, Clutton's joints, or mental retardation. These may be complicated and compounded by maternal drug use.

Using CDC surveillance criteria as descriptors, and with consultation from pediatricians and infectious disease specialists, we defined eight categories of CS presentation. Six categories described infants first identified at the time of birth; two categories chararacterized infants identified after hospital discharge (see box, page 408).

Treatment protocols. Penicillin prevents fetal infection if given during the first trimester of gestation

and usually cures fetal infection if administered before the last month of pregnancy (*13–15*). The current recommended treatment for infants with CS is a 10-day course of penicillin, either crystalline penicillin G daily in two divided doses or procaine penicillin G daily (*15*). Monitoring of the outcome of therapy at 1, 2, 4, 6, and 12 months of age is also recommended, all visits except the first coinciding with the customary well-child care visits, with serologic tests to be performed until they become nonreactive (*16*). Venereal Disease Reference Laboratory (VDRL) tests usually become normal by 6 months of age.

For each of the eight categories of CS presentation, we defined a treatment protocol describing the likely course of therapy during the infant's first year; because some protocols were virtually identical, they were collapsed into a final set of five protocols. Depending on category, protocol components could include hospitalization in a nursery or intensive care unit, outpatient visits, or home health care, as well as diagnostic tests ranging from serology to X-ray and therapy such as antibiotics. Procedures were identified by Current Procedural Terminology (CPT) code (*17*).

Protocols were validated and refined through comparison with the medical charts of infants treated for CS at the Johns Hopkins Hospital during 1991-92. In a procedure approved by the hospital institutional review board, possible CS cases were identified through computer search of discharge abstracts that met the criteria of age younger than 1 year and diagnosis of syphilis (ICD-9A code 090 [congenital syphilis], or 094 [neurosyphilis], or 097 [other unspecified syphilis]). Among 38 infants thus identified, 18 had a maternal or infant history or diagnostic signs consonant with a presumptive diagnosis of CS; 20 cases appeared to have been erroneously assigned a syphilis diagnosis.

Cost of care by protocol. Estimates of the cost of care were calculated from the perspective of a third-party payer such as Medicaid. A cost was computed for each of the five protocols by assigning prices to all clinical services. Hospital daily charges were based on the median 1990 charge among urban hospitals in Maryland, where hospital charges are regulated by the State and are uniform across payers. The average cost of a hospital admission in Maryland in 1990 ($4,640) was less than for other States with large numbers of CS cases such as Florida ($5,312), New York ($6,397), or Pennsylvania ($5,120) (*18*).

Outpatient visits and procedures were priced using relative weights as assigned in the Medicare resource-based relative value system (*19*). A multiplier of $30 per unit was applied to convert each procedure's relative value to a dollar amount comparable to the State of Maryland's 1990 Medicaid fee schedule. As an illustration, table 1 describes the clinical services included in protocol No. 3 and their prices. Because our focus was on costs of treating CS cases (actual or presumptive), we did not include costs of prenatal syphilis screening in our calculation of expenditures. For stillborn infants, we assumed that no costs were incurred for CS treatment.

Table 1. Services, quantities, and prices of a 10-day hospital admission (protocol No. 3) for treatment of congenital syphilis

Clinical service	*CPT code*	*Quantity*	*Unit price*	*Total cost*
Hospital daily care: nursery	N/A	10	$225	$2,250
Lumbar puncture	62270	1	98	98
X-ray upper extremity	73092	1	41	41
X-ray lower extremity	73592	1	41	41
Bilirubin	82251	1	12	12
Drug screen	82660	4	22	88
CSF-glucose	82947	1	7	7
Alkaline phosphotase	84075	1	4	4
CSF-protein	84200	1	8	8
AST (SGOT)	84450	1	4	4
ALT (SGPT)	84460	1	4	4
CBC, platelet, Hgb	85025	1	8	8
CSF, VDRL	86592	1	2	2
RPR	86593	2	7	14
FTA-ABS	86650	2	19	38
FTA-IGM	86651	2	7	14
CSF-cell count	89050	1	18	18
CSF-differential	89051	1	18	18
Physician visit, initial	90225	1	47	47
Physician visit, limited daily	90250	9	27	243
Physician visit, discharge day	90292	1	37	37
Social work counselor	90699	1	26	26
Penicillin IM injection	90788	10	4	40
Total cost of protocol	...	...	...	$3,062

NOTE: CPT = current procedural terminology; CSF = cerebrospinal fluid; AST (SGOT) = aspertate aminotransferase; ALT (SGPT) = alanine aminotransferase; CBC = complete blood count; Hgb = hemoglobin; VDRL = venereal disease reference laboratory; RPR = rapid plasma reagin; FTA-ABS = fluorescent trepanemal antibody-absorbed; IGM = immunoglobulin-M; IM = intramusclar.

Hospital care for CS in Maryland. There is no national source of data describing the case severity distribution among infants diagnosed with CS. As an alternative, we analyzed 1990 hospital discharge abstracts from Maryland hospitals to examine patterns of clinical resource utilization among infants with an ICD-9 code of syphilis. From a file of 69,211 live births, we identified 96 possible cases of CS. Although the discharge abstracts available to us had been stripped of patient identification, demographic

Table 2. Base case assumptions used in the cost estimation procedure for which true values were unknown. For all variables, base case represents the most likely value. Model robustness to the magnitude of each estimate was assessed by varying each parameter across the indicated low to high range

Model parameter	Base case	Sensitivity analysis	
		Low estimate	High estimate
Underreporting of true congenital syphilis cases (percentages)[1]	5	0	10
Presumptively treated cases as percentage of true cases[2]	20	0	100
Case severity distribution—true cases (percentage):[3]			
Protocol 1. Outpatient only	10	0	20
Protocol 2. 5-day hospital admission	15	5	50
Protocol 3. 10-day hospital admission	70	10	90
Protocol 4. 30-day hospital admission	5	0	10
Protocol 5. 365-day hospital admission	0	0	5
Case severity distribution—presumptive cases (percentages):			
Protocol 1. Outpatient only	25	0	50
Protocol 2. 5-day hospital admission	30	5	50
Protocol 3. 10-day hospital admission	45	0	75
Protocol 4. 30-day hospital admission	0	0	10
Protocol 5. 365-day hospital admission	0	0	0
First-year cost of medical treatment for congenital syphilis:[4]			
Protocol 1. Outpatient	$ 657	$ 329	$1,314
Protocol 2. 5-day hospital admission	$2,071	$1,036	$4,142
Protocol 3. 10-day hospital admission	$3,062	$1,558	$6,232
Protocol 4. 30-day hospital admission	$8,156	$4,078	$16,312
Protocol 5. 365-day hospital admission	$91,946	$45,973	$183,892

[1]Adjusts national incidence as reported by the Centers for Disease Control and Prevention (CDC).
[2]Inflates national incidence to account for treated false positive cases not reported by CDC.
[3]Determined random assignment of simulated cases to levels of treatment.
[4]Reflected treatment resource intensity.

Table 3. Base case estimate of national medical expenditures for treatment of congenital syphilis (CS) in 1990

Model parameter	Estimated value
Total first-year medical expenditure for treated cases (rounded to $100k)	$12,400,000
Number of treated CS cases:	
Surveillance cases as reported to CDC	3,484
Unreported true CS cases (under-reporting)	183
Presumptively treated infants (not reported as CS case)	733
Total number of infants treated for CS	4,400
Treated cases by severity category:	
A-1 (mother treated during early gestation)	770
A-2 (mother treated during late gestation)	1,393
A-3 (mother untreated during gestation; infant asymptomatic)	1,503
A-4 (clinically symptomatic full-term infant)	183
A-5 (clinically symptomatic preterm infant)	0
A-6 (infant stillborn)	0
B-1 (asymptomatic infant; identified 1-2 months post-delivery)	367
B-2 (symptomatic infant; identified 3-6 months post-delivery)	183

and geographic codes suggested that 11 of the 96 cases may have been readmissions. The remaining 85 incident cases was similar to the 82 CS cases recorded in Maryland by the CDC surveillance system.

Median hospital charge among the 85 Maryland hospital "incident" CS cases was $3,191 with a median 10-day length of stay. One-half (49 of 85) of cases had hospital charges between $2,000 and $7,000. Only 3 of 85 cases exceeded $10,000 in hospital charges; the most expensive case had a 62-day stay with total charges of $47,142.

Presumptive treatment. Using confidential records not available to us, State health department officials compared the identity of infants with a syphilis-related diagnosis as recorded in the hospital discharge abstract file with the identity of Maryland CS cases reported to CDC. These lists overlapped, but did not match. It appeared that roughly 20 percent of infants recorded by hospitals as having a diagnosis of syphilis at birth were presumptively treated and ultimately did not meet CDC surveillance criteria (Diane Dwyer, MD, Ebenezer Israel, MD, and Betsy Thompson, MD, Epidemic Intelligence Service Officer, assigned to the Maryland Department of Health and Mental Hygiene, supplied this information in a personal communication on December 12, 1992). A possible explanation is that physicians were reasonably aggressive in treating infants who may have had reactive serology due to a mother's previous history

of syphilis. For purposes of cost estimation, this finding meant that the model would need to account for the cost of presumptive care of infants with cases that were not reflected in the CDC surveillance system.

Model construction. To perform the cost estimation, we developed a computer program written in SAS (*A*) that combined data from several input files and generated an output report (see figure). The sociodemographic data file included State-level base year (1990) population by sex and age, number of live births, and stillbirths. The syphilis data file gave reported cases of primary and secondary syphilis and congenital syphilis by State. The protocol file defined the types and quantities of clinical services typically provided to an infant treated for CS according to the category of disease severity. In the price file, each clinical service appearing in a protocol was assigned a cost.

The SAS computer program performed the following sequence of calculations:

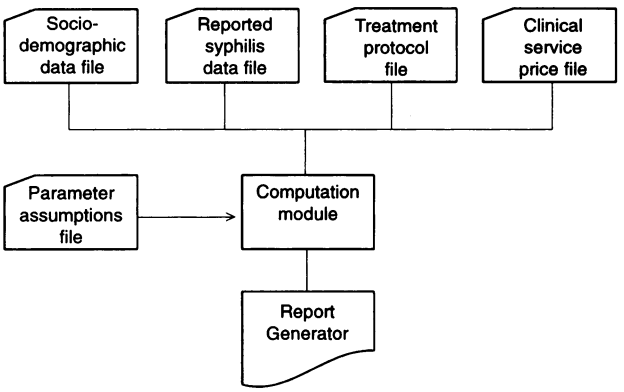
1. Generate an estimate of treated cases by severity level.
2. Assign each case to a treatment protocol as a probabilistic function of severity level to allow for variance within severity levels as well as variation in physician practice.
3. Sum the number of cases treated within each of the five protocols.
4. Multiply the sum of cases within a protocol by the protocol cost.
5. Sum across the five protocols to yield total costs of care.

True values for several important model variables were unknown. These included the relative number of infants presumptively treated for CS in relation to the number of "true" (surveillance) cases, the distribution of treated CS cases by severity, and cost of care. The computer program was structured so that assumptions could be readily varied to facilitate sensitivity analysis. Values used in the model are shown in table 2.

Results

The base case estimate of the national medical expenditure for CS in 1990 was $12.4 million (table 3). In the sensitivity analysis, we varied each model parameter over a wide range to assess its impact on the overall cost estimate. In addition, paired parameters were simultaneously varied to test for interaction effects. Variation in the number of presumptively treated infants relative to the number of treated true cases had little impact on total costs. Similarly, the model was relatively insensitive to change in the price of medical services across a wide range. However, results were sensitive to the severity distribution of true cases. Estimates of total expenditure ranged from a low of $6.2 million to a high of $47.0 million.

Schematic of cost estimation computer program



Discussion

In the past few years a substantial increase in the risk of CS has occurred in several large urban communities in the United States. For example, New York City reported approximately 60 cases per year between 1980 and 1986, whereas 1,017 cases were reported in 1989 (*20*). Although some of this increase was due to a change in the surveillance definition of the disease, it seems clear that a real change in the number of cases has occurred unrelated to reporting criteria (*21*). As evidence, the number of cases of primary and secondary syphilis among women of childbearing age reported in New York City rose from 541 cases in 1986 to 1,841 cases in 1988, a 240 percent increase. Large numbers of CS cases have been reported from States other than New York with high rates of primary and secondary syphilis among adolescent and adult females. For example, CS cases reported in 1990 by States with large urban populations included Florida (591), California (222), Texas (210), Pennsylvania (196), and Illinois (183). Cases were especially concentrated in populations with high rates of drug use and other causes of social disruption (*1*).

Although the number and geographic distribution of CS cases are well-documented, expenditures attributable to this disease are not systematically recorded. Modeling is an approach to filling this void.

Categorization of Congenital Syphilis Cases

Case identified at delivery

Category	*Status of mother at delivery*	*Diagnostic status of infant*
A-1:	Positive; treated during 0-19 weeks gestation	Reactive or nonreactive RPR asymptomatic
A-2:	Positive; treated during 20 and more weeks gestation	Reactive or nonreactive RPR asymptomatic
A-3:	Positive; untreated or inadequately treated during gestation	Reactive or nonreactive RPR; clinically asymptomatic; single abnormal laboratory test (that is, abnormal long bone X-ray, elevated bilirubin)
A-4:	Positive; untreated or inadequately treated during gestation	Reactive or nonreactive RPR; full-term infant; clinically symptomatic (for example, thrombocytopenia, rash, hepatosplenomegaly)
A-5:	Positive: untreated or inadequately treated	Reactive or nonreactive RPR; preterm infant; clinically symptomatic
A-6:	Positive; untreated or inadequately treated	Gestation > 20 weeks or weight 500 grams; stillborn

Case identified post-hospital discharge

Category	*When case identified*	*Status of mother*	*Status of infant*
B-I	During scheduled followup (1-2 months post-delivery)	Positive serology	Reactive or nonreactive RPR, asymptomatic
B-II	After appearance of symptoms (3-6 months post-delivery)	Positive serology	Reactive or nonreactive RPR; symptomatic

RPR = rapid plasma reagin.

However, our analysis has several important limitations. Potential bias stems from the reporting mechanism itself. Underreporting may be present in many localities, which would result in our estimates being low. Counteracting this underreporting is the new case definition which has resulted in the inclusion of many low-risk cases. The standard of care observed at the Johns Hopkins Hospital, which was the basis for treatment protocols, may not reflect practice patterns across the nation.

Our cost estimate includes only first-year direct medical costs, although reports indicate that some infants with severe cases of CS require long-term care. Types of care required include special education, when the main effect of CS is learning disability, and even lifetime custodial care, if CS results in profound physical and mental disability (*21–24*). Underreporting (until recently) of CS limits the availability of accurate etiologic data on children now in school (*4*).

To gain insight on the frequency of severe cases, we informally surveyed pediatric infectious disease specialists in the high prevalence areas of New York City, Baltimore, and Washington, DC. None reported having treated such a case. Even with accurate information on severe cases, cost attribution would be difficult since these infants are typically impaired by maternal drug abuse, maternal smoking, prematurity, and nutritional deficit (*25*).

Our model suggests that the relative number of infants receiving presumptive treatment for CS has little impact on the total national medical expenditures for the disease. On this basis, we believe physicians are correct in aggressively treating newborns when there is any reason to suspect CS. Unlike many conditions, where "aggressive" is synonymous with expensive care, aggressive treatment of CS entails a relatively cheap 10-day course of penicillin. Many infants now remain in the hospital to ensure compliance with a typical 5–10-day treatment regimen.

Inpatient care represents a substantial expense—from $1,500 to $3,000 by our estimate. Outpatient visits are far less expensive, but mothers may find it

difficult to return for 10 sequential daily visits. Some centers have found that use of home health nurses to administer daily penicillin injections is a cost-effective alternative which has the additional benefit of an opportunity to counsel the mother on postnatal care (personal communication, Ted Hendershot, MD, Division of Disease Control, Philadelphia Department of Public Health).

Because CS cases are concentrated in a few major urban centers, expenditures for this disease could be dramatically reduced through carefully targeted interventions. These interventions would include well-established public health programs of prenatal care and screening and treatment of these high-risk populations in addition to control of sexually transmitted disease. In this scenario, when an infected male is diagnosed, disease intervention efforts (that is, contact tracing) to identify and treat potentially infected females (the sexual partners) would prevent most CS, since we can assume that some of the female partners would be pregnant as well.

Estimating the cost-effectiveness of CS prevention is difficult because, ideally, it is a component of comprehensive prenatal care. Nearly all CS is preventable by screening and treatment during the prenatal period. Conversely, CS cases have been highly associated with little or no prenatal care. Provision of prenatal services would have substantial impact which should not be isolated from the other benefits of adequate maternal care on healthy outcomes of pregnancy.

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Equipment

A. SAS statistical software version 6.03. SAS Institute, Inc. Cary, NC