The Half-Life of Cost-of-Illness Estimates: The Case of Spina Bifida

Norman J. Waitzman, Ph.D.
Department of Economics
University of Utah
Salt Lake City, UT

Patrick S. Romano, MD, MPH
Division of General Medicine and Section of General Pediatrics
School of Medicine
University of California, Davis
Sacramento, CA

Scott D. Grosse, Ph.D.
National Center on Birth Defects and Developmental Disabilities
Centers for Disease Control and Prevention
Atlanta, GA

Introduction

Neural tube defects, which include spina bifida, are one of the most frequent and important categories of birth defects. Accordingly, there has been considerable interest in studying the impact of spina bifida as a public health problem. This impact can be measured in various ways, including disease-specific mortality, morbidity, functional limitation or disability, and quality of life impairment. Each of these measures captures one component of the total burden of disease. Such measures of impact are important because they allow public health agencies, researchers, and health care providers to understand the effects of preventive or diagnostic interventions, changes in disease incidence or prevalence, and new technologies.

In recent years, cost-of-illness estimates have been widely used. The cost of illness reflects both the direct costs of providing medical care, rehabilitative care, developmental services, and special education to affected children, as well as the so-called indirect costs of reduced workforce and household productivity. All of these costs contribute to the total economic burden of spina bifida.

Generating cost-of-illness estimates is not a trivial exercise. Nearly a decade ago, we authored the most widely cited and carefully developed estimates of the cost of spina bifida and several other birth defects (Waitzman, Romano and Scheffler, 1994; CDC, 1995; Waitzman, Scheffler and Romano, 1996). This work has been widely used in economic evaluations of ultrasonography (Waitzman and Romano, 1998; Vintzileos et al., 1999; Vintzileos et al., 1998a; Vintzileos et al., 1998b), folic acid supplementation and fortification of foods with folic acid to prevent neural tube defects (Postma et al., 2002; Romano et al., 1995; Kelly et al., 1996), and other interventions (Rouse and

Stringer, 2000; Chung et al., 2001; Vintzileos et al., 2000; Randolph, Hartshorn, and Washington, 1996).

Our analysis of birth defect cost involved analyzing fifteen data sets over a period of two years, and required over $200,000 in financial support from the California Birth Defects Monitoring Program, as well as support from the Agency for Healthcare Research and Quality through training grants to the first and second authors. An effort of this magnitude is unlikely to be replicated in the near future. Therefore, it is important to consider the half-life of these estimates. In other words, are the estimates that we generated nearly a decade ago still valid? Can they be adjusted in a "back-of-the envelope" fashion to reflect current prices? If so, how? If not, why not? What factors need to be considered before deciding whether to undertake a new study, versus simply updating estimates from an old study?

In this chapter, we establish a simple framework for determining the continued validity of cost of illness estimates. We find that cost-of-illness estimates remain valid so long as certain conditions and assumptions do not fundamentally change. We then apply that framework to our estimates of the societal cost of spina bifida. Adjusted estimates of the cost of spina bifida per case in the United States are provided based on this exercise.

A General Framework for Assessing Validity of Cost-of-Illness Estimates

Cost-of-illness estimates may grow obsolete due to factors characterized as "internal" to the disease process. Such factors include changes in treatment patterns, reimbursement, or prevalence for the condition of interest. Developments in statistics, economics, and epidemiology that establish the theoretical underpinnings and methodological approaches for estimating cost of illness, however, can also make

estimates of cost obsolete. Such "external" factors might be as rudimentary as the availability of more reliable data or as involved as the emergence of a new consensus about the disease process that reveals a misattribution of cost because co-morbidities or related conditions were previously not fully understood. Also, new analytic methods could render older estimates obsolete. For example, within economics, there is continued debate over the validity of the human capital or "livelihood" approach that has traditionally been used in cost of illness studies, including our own, relative to the willingness-to-pay approach, which has firm foundation in theoretical welfare economics (Garber et al., 1996; Rice et al., 1990). New statistical techniques for estimating and predicting costs are also being developed that may be superior to their predecessors for specific purposes, such as predicting future costs (Lipscomb et al., 1998).

For the current analysis, we develop and apply a framework that relates strictly to "internal" factors. The methodological and theoretical underpinnings of our birth defect cost estimates are still widely accepted and applied (Luce et al., 1996; Haddix, Corso, and Gorsky, 2003). An exception to such neglect of external factors in the current analysis is the integration of a new discount rate to our estimates in response to the recommendations from expert panels on the use of cost-effectiveness techniques (Lipscomb, Weinstein and Torrance, 1996; Corso and Haddix, 2003).

The critical internal factors that drive change in costs include changes in treatment, transaction prices,[1] and prevalence. Patterns of treatment may be altered in

[1]Transaction prices are those actually used for reimbursement. List prices, incorporated into "billed charges," are not appropriate to apply in cost-of-illness studies, as reimbursement for medical care, often through third-party payment, is based on negotiated discount or "transaction" prices that more accurately reflect the true societal or "opportunity" costs of treatment. The myriad number of "transaction prices" for any given service poses a challenge for cost-of-illness investigators. Medicare reimbursement rates were adopted as the standard in our study (Waitzman, Scheffler, and Romano, 1996), as such rates are widely accepted and based on detailed evaluation of underlying resource use.

response to the development and diffusion of new technologies, the acquisition and application of new information, the passage of new legislation or regulation, or other changes in the organization and delivery of services. Changes in prices will change the nominal outlays for services (direct costs, or resources used), whereas changes in labor compensation will affect the nominal level of indirect costs (resources lost due to heightened morbidity and premature mortality). Prevalence may change as a result of changes in survival or longevity of affected individuals, introduction or diffusion of prevention strategies, or application of new screening techniques that change the incidence of the condition through higher rates of termination of pregnancy.

More formally, these three general components driving change in cost of illness can be expressed in a simple model of prices (P), quantities (Q), and Prevalence (N). The total societal cost of an illness, TC, such as spina bifida, can then be expressed as

1) $TC = \Sigma_j AVG_j \times N_j$

where AVG is the average cost per case for the N number of affected individuals/cases in each jth age/demographic/severity/or other relevant category used for stratification. Furthermore, the average cost per case can be expressed as

2) $AVG_j = [\Sigma_i P_{ij} \times Q_{ij}]/N_j$

where P is the transaction price, Q is the quantity of treatment used (direct costs) or productivity lost (indirect cost) for each category of cost, i, for affected individuals in each jth group above. For example, if i is the category, inpatient medical care, and j indicates the age category encompassing the first year of life, then the average cost of illness for this group is simply the price of services multiplied by the quantity of services provided to all infants with the condition divided by the number of such infants. This

simple framework provides a straightforward way to characterize the sources of obsolescence in cost estimates, and each is addressed in turn.

Changes in Prices (P)—To the extent that costs of illness change due to changes in prices (P), cost estimates adjusted for price inflation remain valid as long as the price index used accurately captures price changes. This may be problematic because of differential rates of price inflation across goods and services and because of the inherent difficulties in separating price changes from quality changes owing to continual change in the characteristics and mix of goods and services. Furthermore, any specific price index is limited by the scope of the underlying sample that is used to generate it. For example, estimates of medical costs are often adjusted for inflation using the medical care component of the consumer price index (MCPI), as in the current study, but that index is weighted strictly by the quantity of, and transaction prices for, services that consumers pay out-of-pocket. The MCPI therefore ignores the substantial payments made by public entities in medical care, as well as the transaction prices paid by third-party payers.

Even without such sampling difficulties, inflation can vary dramatically among different types of medical products and services. For example, between 1988 and 2002, the overall MCPI increased by 106%, while the inpatient component of the MCPI increased by 156%. Valid estimates require that cost figures are updated using appropriate price indices that are refined enough to capture the price changes of interest. More specifically, the price index in which the price for a specific service, P_i, falls must accurately summarize and appropriately weight the change in service or cost category, i, of interest. One should not assume that even disaggregated price indices capture inflation correctly. For example, using the inpatient sub-component of the MCPI to adjust the

inpatient component of medical costs of spina bifida involves two implicit assumptions: first, that that sub-component accurately summarized general inpatient price increases and second, that the inpatient services generating the increase in spina bifida costs are appropriately weighted in that component of the MCPI.

Estimates of indirect costs, or productivity losses, need to be similarly updated for changes in the compensation of labor. The Employment Cost Index (ECI), calculated by the Bureau of Labor Statistics for the civilian workforce, captures fringe benefits, including health insurance coverage, as well as wages and salaries paid by employers. Sub-components of this index capture compensation changes for sectors of the workforce.

Changes in the Number of Affected Individuals (N)—A general change in incidence (N) of a condition will affect total cost estimates, TC, but will leave per case estimates, AVG, unaffected. Total societal costs can therefore be accurately re-estimated using AVG, as long as accurate data are available on change in N. Per case estimates, however, will lose validity if the following three conditions are all met: the change in incidence resulted from a change in the weight of a specific stratum N_j within overall prevalence, N; the grouping N_j was associated with significant variance in cost; and the original estimates of cost per case, AVG, ignored this particular jth factor. For example, location of the spina bifida lesion (thoracic/high lumbar, low lumbar, and sacral) is associated with differences in average costs, which was not formally addressed our original cost study. If mandated fortification of grains with folic acid changed the birth prevalence of spina bifida across level of lesion, then per case cost estimates could be affected. Other interventions that may have changed birth prevalence, such as more

refined prenatal diagnostic tests that lead to selective termination of pregnancy based on severity, could have a similar effect.

Changes in Treatment (Q)—Our estimates of spina bifida costs were based on treatment actually delivered to persons in California rather than on some gold standard of what ought to be provided. Changes in treatment modalities will almost invariably compromise the validity of cost estimates per case, AVG, as well as estimates of total cost, TC. While an obvious source for such change is the advent and diffusion of new medical technologies, there are other important potential sources both within and outside of medicine. Within medicine, changes in the organization of medical practice under managed care, changes in reimbursement practices, and legislative changes to Medicaid and Medicare, all potentially affected the incentives faced by providers over the past decade and thereby could have led to new treatment patterns for children with spina bifida. Expenditures on special education and developmental services could have changed as well due to changes in medical care, but also in response to changes in the funding and administration of such services. Changes in labor market participation by those with disabilities would similarly affect indirect cost estimates.

It is worthwhile to consider the conditions under which the validity of cost estimates is most at risk due to changes in treatment modalities (Q). If the change was strictly an add-on (a new service, "i") that had no effect on other service delivery requirements, for example, then previous cost estimates need only be enhanced by estimates of costs associated with the new service. This is the case for categories of service that were neglected in the original estimates as well as for new services that leave other treatment patterns unchanged.

Because medical care service costs represent such a large proportion of our estimated costs of congenital anomalies, and because those services affect later requirements for special education and developmental services, as well as productivity in the labor market, changes in medical care services will more drastically shorten the half-life of cost-of-illness estimates than will changes in other "non-core" treatment areas. Even so, this half-life may be lengthened or shortened depending on whether or not treatment patterns change strictly for a specific jth sub-population with the condition. If insurance status changed for a particular sub-group with the condition, such as uninsured patients, so that the treatment now received by that group more closely approximates that delivered to another sub-group, then cost estimates could potentially be adjusted without generating comprehensive new estimates, depending once again on the level of refinement of the original cost estimates.

Applying the Framework: How Valid are Price-Adjusted Spina Bifida Estimates?

Perhaps the most straightforward adjustments that can be applied to old cost estimates are price adjustments (P) to account for inflation. Indeed, it is general practice for researchers using cost estimates to apply some price adjustment for inflation and/or for purchasing power parity. There are other adjustments that would be fairly straightforward to incorporate, among them changes in survival, changes in the percentage with a school or work limitation, and alternative discount rates applied to future costs. But the main focus here is to assess how valid our estimates remain when price-adjustment alone is applied.

We compare our price-adjusted estimates to more recent evidence on the medical costs of spina bifida in the literature and from administrative databases. We also consider

a recent estimate of special education costs for the federally-designated special education category, orthopedically handicapped. Substantial differences with more recent estimates would suggest a short half-life for cost estimates. Close approximation between the estimates, on the other hand, would suggest that treatment patterns may not have changed sufficiently in the past decade to merit the generation of comprehensive new estimates.

For the consideration of price-adjusted medical care costs, we generated comparisons with three distinct sources: a Washington State study that analyzed the distribution of medical costs for certain chronic illnesses, including spina bifida (Ireys et al., 1997); estimates of inpatient costs generated from the 1997 national Kid's Inpatient Database (KID) on pediatric hospital discharges; and 1991 and 2001 claims data from a managed care organization in Utah.

Price-adjusted medical costs, 1993 evidence—A study by Ireys et al (1997) used Washington State Medicaid data to address policy issues surrounding the distribution of medical care expenditures for children with chronic illnesses. Summary data from that study on children up to age eighteen years with spina bifida are given in the first column of Table 1. From our estimates of birth prevalence and survival, we constructed a synthetic sample of all children with spina bifida up to eighteen years of age in California in 1988 to match the subject population used in the Washington study. Summary characteristics for this synthetic sample in California are reported in the second column of Table 1. In terms of demographic characteristics, the average age of the two groups is nearly identical. The Washington sample had a slightly higher percentage of girls, but we have no data on the racial composition of the California sample.

In terms of cost, reported mean Medicaid expenditure for the group in Washington in 1993 was $11,061. Our estimate for the California sample, adjusted to Medicare reimbursements, was $9,924 in 1988. Price adjustments need be made for medical care inflation between 1988 and 1993 and for differences in reimbursement between Medicare in California in 1988 and Medicaid in Washington in 1993. We adjusted reported Medicaid reimbursements in Washington to approximate Medicare reimbursement rates, as explained in the notes to Table 1.[2] Geographic differences in Medicare payments per beneficiary, after adjusting for differences in case-severity and practice patterns, have been shown to largely reflect underlying differences in wages and costs of living (Medicare Payment Advisory Commission, 2003). We therefore adjusted the Medicare-anchored California and Washington estimates to the United States as a whole.[3] Finally, the 1988 estimate was adjusted to 1993 medical care prices by applying changes in the inpatient component and "all other" components of the MCPI according to the percentage weights of such care in the original estimates. The resulting figures, reported in the final row of Table 1, are once again very similar to each other, $14,607 based on the Washington data, and $13,773 based on our California estimates. The difference between the two estimates could be attributable to residual price differences,[4] as well as to differences in the spina bifida case mix between Washington's Medicaid program in 1993 and California in 1988.

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[2] Medicare reimbursement levels were used to approximate underlying cost (see footnote 1).

[3] We re-normalized state cost of living estimates from Berry, Fording and Hanson (2000), which were normalized to cost of living in Texas in 1960, to annual national national cost of living averages, using intercensal state population estimates as weights. The resultant cost of living adjustments were .965 and 1.083 for Washington in 1993 and California in 1988, respectively.

[4] Lower cost of living adjustments for California or higher ones for Washington would have resulted in still closer estimates. Two other sets of state cost of living estimates using slightly different methodologies (Nelson 1989; McMahon 1991), generated 1988 values for California centered on the Berry, Fording and Hansen (2000) estimate adopted here, but provided uniform support for higher Washington state values.

Price-adjusted medical costs, 1997 evidence—The Health Care Utilization Project of the federal Agency for Healthcare Research and Quality includes a national dataset on pediatric hospital discharges from 22 states, the Kid's Inpatient Database or KID. The 1997 KID was used to estimate total inpatient costs for those aged 0-1 years with spina bifida. Weights on the dataset permit national estimates. National cost-to-charge ratios for urban and rural hospitals applied to that data yielded a total national cost of $60,136,566 for discharges among children below 24 months of age for whom spina bifida was listed as a diagnosis. KID does not contain unique individual identifiers, so it is not possible to link discharges for the same individuals or calculate total hospital costs for an individual child.

Because no prevalence data were available from KID, a denominator had to be constructed to estimate average inpatient costs. Using a complex algorithm, Jim Robbins and Mick Tilford of the University of Arkansas for Medical Sciences calculated that the 1997 KID weighted data covered an estimated 1,387 infants with spina bifida (personal communication). Assuming a comparable number of births in the previous year and assuming 90% survival to one year of age (Wong and Paulozzi, 2002), we estimated the there were 2,566 children less than twenty-four months of age with spina bifida in 1997. Using this denominator yielded an average inpatient cost of $23,436.

Our estimate of acute inpatient costs per case for the same age group in California, adjusted to 1997 using the hospital services component of the MCPI and adjusted for cost of living differences between California and the nation as a whole, yielded $28,151. But California inpatient care estimates from discharge data used in our study were enhanced based on our detailed analysis of a comparative subset of

longitudinal data demonstrating that many hospital discharge abstracts did not list spina bifida as a primary or secondary diagnosis because the diagnosis was not made until after discharge, or because the diagnosis was simply left off the hospital record. For the age group under consideration, this enhancement factor was 1.03 for California discharge data. Applying a final adjustment to our estimate due to the absence of such an enhancement factor on the 1997 national discharge data yielded $27,331, still nearly $4,000 more than the corresponding estimate from the KID data.

One likely source of this $4,000 discrepancy is an underestimate of the enhancement factor when applied to national data. California hospital discharge abstracts have twenty-one fields for diagnostic reporting, whereas nearly all other states have fewer fields. Use of discharge abstracts from such states would therefore require a larger enhancement factor than was applied to estimates based on California discharge data.

Another factor that may have contributed to the reported discrepancy between the 1997 KID estimates and the adjusted hospital cost estimates from California was the national trend between 1988 and 1997 away from inpatient care toward greater reliance on outpatient care. Note that this was not as much of a concern in the Washington/ California comparison provided in Table 1 because that comparison was based on a comprehensive set of medical services rather than just one component of medical services. To the extent that inpatient services were substituted with equivalent outpatient services, overall medical care estimates were unaffected. Indeed, Ireys et al. (1997) reported that 51% of medical services delivered to those with spina bifida under Medicaid in Washington in 1993 were provided on an inpatient basis. This compares with 58% in 1988 for the comparable California sample. To the extent that this

difference in the locus of care reflects a real and general trend, then it could explain a significant part of the $4,000 discrepancy above could be attributable to that shift.

A related concern is the sensitivity of inpatient cost estimates to the choice of index for medical service price adjustment. Our adjusted estimate would be $23,945 instead of $27,331 if the general MCPI were used to inflate inpatient medical care estimates rather than the hospital services component of the MCPI. To the extent that there had been a shift in the locus of care from inpatient to outpatient services for spina bifida treatment that mirrored the general shift in locus of care in the country between 1988 and 1997 (Levit et al, 2004), the weight of the inpatient component in the overall price adjustment ought to be reduced, and the resulting estimate based on California data would be lower. As discussed below, estimates of the cost of spina bifida for 2002 given in Table 2 provide a sensitivity range based on different assumptions regarding the mix of inpatient and outpatient services for those with spina bifida and the correct application of corresponding medical price indices for the period 1988 to 2002.

Price-adjusted medical costs, 2001 evidence—We performed preliminary analyses of comprehensive claims made available to us on spina bifida patients in 1991 and 2001 covered by a single, major insurer in Utah. These data included a detailed breakdown of all medical care services by type of service and associated billed, allowed, and reimbursed charges by age group. The relatively small number of spina bifida patients limited our ability to perform detailed analyses, particularly when restricting the sample to those enrolled in the plan continuously for an entire year. Still, certain aggregations of the data provided insights related to price-adjusted medical care estimates for spina bifida.

First, the data firmly established that the ratio of overall payments for medical care services provided for individuals with spina bifida to the subset of encounters where spina bifida was listed on claim records was consistently greater than 2.0. Furthermore, this ratio did not appear to be systematically different for outpatient versus inpatient services. This result reinforced the finding that cost estimates for spina bifida that rely strictly on the appearance of a diagnosis code in claims or discharge data, as with the estimates from the KID study, will likely underestimate the true costs of the condition.

Second, age-specific estimates of overall medical care costs from the 1991 data, when adjusted by the MCPI to 2001, fell within 10% of actual expenditures for their counterparts in the 2001 data. This suggested a lack of change over time in patterns of health care utilization for patients with spina bifida in a relatively homogenous population. On the other hand, outpatient services as a percent of total medical care services provided to each age group appeared to increase, mirroring the trend in the nation. These results are tentative for the following reasons: changes in coding conventions need to be further examined; the existence of outliers coupled with a relatively small sample made some results unstable; and the effects of dual coverage and of Medicaid managed care coverage within the system in 2001, have not yet been established.

Price-adjusted special education costs, 2000 evidence— Orthopedic impairment is the primary category among the eleven federally designated eligibility categories to which children with spina bifida requiring special education services are assigned. Recently published data on special education costs provided from the Special Education Expenditure Project (Chambers, Schkolnik, and Perez, 2003) found that the average

special education expenditure per pupil in the orthopedic impairment category was $14,993 (95% confidence interval, $13,398 to $16,588) for the United States in 2000. Our estimate of the average per pupil special education cost for those in the orthopedic impairment category in California was $11,110 in 1988. When adjusted for the increase in the employment cost index (ECI) for primary and secondary schools between 1988 and 2000, and for the estimated cost of living difference between California and the United States in 1988, our price-adjusted estimate for the nation in 2000 was $15,288. The remarkable similarity between price-adjusted estimates from our study and estimates from later work provides support for the view that changes in spina bifida costs have been mainly attributable to price changes. In this case, the evidence suggests that students within a particular handicap category received similar services in 2000 as they did in 1988. Average special education costs for children with spina bifida could still have changed since 1988 due to changes in the overall proportion with the condition receiving special education services or due to changes in the allocation of those receiving services across federal handicap categories, but we have no information on that.

Summary assessment of price-adjusted costs—When our 1988 medical care and special education cost estimates were carefully reconstructed to match as closely as possible available evidence from the literature and from selected databases, both before and subsequent to our estimates, and when those estimates were subjected to refined price-adjustments, our adjusted estimates were remarkably similar to recent evidence. Thus, our cost estimates, when carefully subjected to price adjustments, appear to still be useful for evaluating interventions and programs that are expected to affect the incidence or prevalence of spina bifida. This conclusion is not surprising considering that the

current practice of surgical closure of the spine and the placement of shunts for hydrocephalus for those born with spina bifida was also general practice in 1988 when our cost study was conducted (http://www.spinabifidamoms.com/english/overview.html#1, 2003).

Given the evidence for their continued validity, we provide price-adjusted estimates for 2002 by detailed direct and indirect cost category in Table 2. These figures adjust for cost of living differences between California and the nation applied to our original estimates (column A), the application of a 3% discount rate to costs beyond the first year of life (column B), and increases in price indices applied to the 1988 estimates in column B to arrive at a range of estimates for 2002 (columns C1-C3) based on a sensitivity analysis.

The sensitivity analysis was generated to demonstrate the adoption of different assumptions regarding the hospital/non-hospital case mix of medical care services when applying different component parts of the medical care consumer price index to medical care costs. Medical cost figures in column C1, for example, reflect the application of the increase in the overall MCPI, which implicitly assumes that the case mix for spina bifida is identical to the average mix of care in the country across all conditions. This assumption is clearly incorrect, as our data showed significantly higher inpatient utilization of services than average for treatment of spina bifida. But the figures are provided as an illustration because it is often general practice to price-adjust using the general MCPI, ignoring differences in mix of services. The medical care cost figures in column C3, on the other hand, reflect an assumption that the hospital/non-hospital mix of services provided for treatment of spina bifida has not changed significantly since 1988.

The resultant estimate may be too high, as there has been a general shift of services from inpatient to outpatient settings since 1988, and medical care prices have risen far more for inpatient medical care services than for other medical services.

Price-adjusted medical cost figures in C2 reflect an assumption of higher inpatient delivery of services for those with spina bifida than for the general population, but a shift in venue for such treatment since 1988 equivalent to that for the nation as a whole. This represents our best estimate. The resultant per case estimate in the United State of $635,763 in 2002 using a 3% discount rate for costs beyond the first year is almost 2.75 times the original estimate for 1988 using a 5% discount rate. Most of the increase was due to price/compensation increases between 1988 and 2002. The change in discount rate disproportionately enhanced indirect cost estimates, given the prolonged period after birth before the bulk of labor market and household productivity losses are incurred.

The remainder of the current analysis is devoted to a brief discussion of potential add-ons to these cost estimates, to changes in technology that threaten to shorten the half-life of our price-adjusted estimates, and to changes in prevalence.

Costs and Changes in Treatment (Q) due to Add-ons and Changes in Technology

Changes in Cost due to Q, Add-ons—While the evidence presented thus far supports the use of price-adjusted estimates of spina bifida costs given in Table 2, there are add-ons that could enhance these estimates and changes in technology that potentially threaten to make such estimates obsolete. Most add-ons relate to categories of resource use that were neglected in our study rather than new treatments incorporated into practice since 1988. Perhaps the most significant neglected category was parental care-giving cost, that is, the value of additional time by parents devoted to care for a child with spina

bifida relative to that given to the average child. Such cost was estimated by Lipscomb (1986) based on a survey of 104 parents of children with spina bifida conducted in North Carolina in the early 1980s showing substantial reductions in earnings due to fewer hours worked per week for both mothers (14 hours) and fathers (5 hours). These figures are likely overestimates due to the nature of the survey. They were included in the cost estimates for spina bifida reported by Kelly et al. (1996), along with figures on direct costs taken from our earlier study.

Our estimates of cost also did not include any incremental cost associated with the medical services used in the delivery of the newborn, as such costs appeared on the maternal discharge record rather than that of the infant. Some incremental costs of delivery were therefore missed, as the rate of Cesarean section in 1988 was likely already higher for newborns with spina bifida than for the average newborn. Currently, delivery by Cesarean section is standard practice for newborns who are prenatally diagnosed with spina bifida, and so the incremental cost associated with such delivery is an appropriate add-on to our direct medical cost estimates.

The event that conditioned our cost estimates was live birth with spina bifida. Costs were assumed to be zero up to that event. Additional costs would be appropriate to include if the standard that was applied was total cost contingent on *detection* rather than *birth*. The proliferation of prenatal screening, together with more sensitive screening for congenital anomalies, has increased prenatal detection of spina bifida. Prenatal detection has affected cost through the selective termination of pregnancy and the resulting birth prevalence of spina bifida. But to the extent that prenatal detection has led to more service delivery in preparation for live birth, including delivery by Cesarean section, all

such incremental prenatal services costs would be appropriate to include as an additions to our direct cost estimates of medical care.

Changes in cost due to new technology—The surgical closure of the spine in-utero began in 1994 on a very selective basis, and only a few hundred such surgeries have been performed, all in four hospitals in the United States (www.fetal-surgery.com, 2003). The procedure is now the focus of a five-year, randomized trial, funded by the National Institute for Child Health and Human Developmen (NICHD), underway at three centers: University of California, San Francisco; Children's Hospital of Philadelphia; and Vanderbilt University. The potential benefits cited in the literature of such surgery are prevention of some neurological loss associated with exposure to the intrauterine environment, and prevention of the Arnold-Chiari II malformation of the brain with subsequent avoidance of shunts for hydrocephalus (Olutoye and Adzick, 1999). If such surgery proves to be effective and is adopted as general practice, it would likely radically alter the treatment of spina bifida and render our cost estimates obsolete. Subsequent estimates of the cost of spina bifida would also have to include the additional risks to maternal health associated with fetal surgery, which presents additional challenges with respect to data collection and estimation of both direct and indirect costs.

Prenatal screening, as noted previously, is a technology that has become more widespread. Some portion of such costs could be treated as a cost of spina bifida, but its incorporation is potentially more complicated. If prenatal detection of spina bifida results in termination of pregnancy, the cost of spina bifida is potentially affected by the ensuing cascade of events, such as a subsequent pregnancy intended to "replace" the terminated pregnancy that was affected by spina bifida (Waitzman and Romano, 1998). In addition,

if prenatal care is included, it would also be logical to include public health efforts to address the impact of spina bifida, which would include folic acid fortification, promotion of supplement use during pregnancy, and surveillance and research into additional risk factors, which would not be affected in the short-term by changes in the birth prevalence of spina bifida.

Changes in Incidence and Survival (N)

Selective termination poses the problem cited in the framework provided earlier if resulting birth prevalence changes in a way that alters the composition of costs. For example, if screening resulted in an increased likelihood of termination of the most severe cases of spina bifida, and cost estimates were not made according to severity, then both direct and indirect cost per case estimates would suffer some distortion because average treatment patterns changed as did the average profile of survival and disability.

Recent data from the Metropolitan Atlanta Congenital Defects Program (MACDP) have demonstrated a steady improvement in survival among infants with spina bifida over the period from 1979 through 1994 (Wong and Paulozzi, 2001). Survival to one year of age was 82.7% in the 1979-83 birth cohort, 88.5% in the 1984-88 birth cohort, and 91.0% in the 1989-94 birth cohort. By comparison, our published estimates of the cost of spina bifida were based on observed one-year survival of 80.3% in the 1983-86 California birth cohort. Wong and Paulozzi's exclusion of infants with trisomy 13 or 18 accounts for only about 3% of the 8% difference in survival between contemporaneous birth cohorts in the MACDP and California data, suggesting that there may also have been geographic differences in patterns of care and surgical outcomes. It is not clear whether there have been any recent changes in survival beyond the first year

of life. Our analysis assumed 95% survival to five years of age, among children who survived infancy while Wong and Paulozzi reported 92%. We suspect that these estimates are effectively equivalent, given the relatively small number of deaths upon which they are based.

Applying Wong and Paulozzi's updated estimate of 91.0% first-year survival to our earlier analysis of the cost of spina bifida would increase aggregate direct costs for medical care and special education services beyond the first year, but decrease aggregate indirect cost. The close proximity of our price-adjusted cost estimates to more recent estimates suggests that these improvements in survival, to the extent that they have occurred, have not been associated with significant changes in the average level of service requirements by age.

Conclusion

This analysis has provided a framework for assessing the validity of cost-of-illness estimates from the vantage point of factors "internal" to the disease process such as treatment patterns, prices, and prevalence. Our estimates of the cost of spina bifida in California in 1988 were subjected to that framework. Evidence from this exercise suggested that price-adjusted estimates, when carefully constructed, have maintained their validity. While the continued accuracy of the adjusted estimates may be adequate, they could be significantly enhanced by estimates of certain additions, particularly caregiver costs, which were neglected in our original study. The price-adjusted per case estimates provided in column C2 of Table 2 may be used with some confidence in evaluations of interventions that are likely to affect the birth prevalence of spina bifida, but such estimates are likely conservative due to the omission of certain costs.

The most profound change with respect to the societal costs of spina bifida over the past decade was the reduction in birth prevalence and subsequent cost probably due to fortification of foods with folic acid. In other words, this public health measure had a more profound impact on the total cost to society of spina bifida than did changes in medical care technology. This will not necessarily be the case in the upcoming decade, as the introduction of new technology, such as fetal surgery, may revolutionize treatment patterns for the condition. The continued development and diffusion of prenatal screening technologies also have implications related to the selective termination of pregnancy and potential alteration of the distribution of cases across severity categories. Evaluation of future interventions that affect the birth prevalence of spina bifida may therefore require greater precision with respect to some subset of cases than is possible with the adjusted per case estimates provided in Table 2. New estimates that more carefully account for the variation in costs according to clinical features may therefore be required even if our estimates of average cost remain valid.

Table 1. Medical costs of spina bifida taken from Washington State Medicaid data in 1993 compared to adjusted California estimates from 1988.

Study / Comparative Data	Washington	California
Sample		
Mean Age (years)	8.3	8.25
% female	56	53
% non-white	32	Not available
Cost		
Raw Mean ($)	11,061**	9,924**
Price and cost of living-Adjusted Mean	**14,607*****	**13,773*****

* Raw data on prevalence and survival in California from Waitzman, Scheffler, and Romano (1996) were used to generate a "synthetic" prevalent population in California to compare to the zero to eighteen year-old sample used in Ireys et al. (1997). Statistics provided in the column are from this synthetic population.

** Figures in the first column reflect actual Washington State Medicaid expenditures in FY 1993, whereas the second column counterparts are 1988 California estimates adjusted to Medicare reimbursement rates in that state.

*** Figures in the first column are adjusted to Washington Medicare reimbursement rates and to the United States based on cost of living data. The federal Prospective Payment Assessment Commission (1991) reported that Medicare and Medicaid reimbursed at 100% and 77% of hospital costs, respectively, in Washington in 1989. The federal Physician Payment Review Commission reported that Medicaid reimbursed physicians from 76% to 83% of Medicare fees in Washington in 1993 (PPRC, 1994). Figures in the second column, already adjusted to Medicare payments, are adjusted to the United States based on cost of living data (Berry, Fording and Hanson, 2002) and to 1993 prices using weighted sub-components of the medical care component of the consumer price index.

Table 2. Average Lifetime Cost per Case of Spina Bifida ($), United States, with selected adjustments by cost category

Cost Category	(A)* 1988, 5% discount	(B)** 1988, 3% discount	(C1) 2002, 3% discount with sensitivity analysis for medical care inflation***	(C2)	(C3)
DIRECT COSTS					
Medical Inpatient (Gross)	*62,359*	*76,275*	*157,127*	***161,805***	*195,264*
Medical Other (Gross)	*43,421*	*54,935*	*113.166*	***123,769***	*99,982*
Medical Total (Net)	89,869	107,067	220,560	**235,839**	245,511
Special Education	21,089	25,836	41,337	**41,337**	41,337
Developmental Services	900	1,245	2,034	**2,034**	2,034
Total Direct	111,858	134,138	263,931	**279,210**	288,882
INDIRECT COSTS Heightened Morbidity	47,614	95,893	138,086	**138,086**	138,086
Premature Mortality	74,676	151,720	218,477	**218,477**	218,477
Total Indirect	122,290	247,613	356,553	**356,553**	356,553
TOTAL COST	234,148	381,761	620,484	**635,763**	645,435

* Figures in Column A are California per case cost estimates from Waitzman, Scheffler, and Romano (1996) adjusted to the United States by dividing direct costs by a 1988 cost of living adjustment factor, 1.083 (Berry, Fording and Hanson, 2000) and indirect costs by the ratio of average employee compensation in California to such compensation in the nation in 1988, 1.103.

** Figures in Column B are those in Column A applying a 3% discount rate to costs beyond the year of birth rather than 5%, as recommended by expert panels on performance of cost-effectiveness analyses (Lipscomb, Weinstein and Torrance, 1996; Corso and Haddix, 2003).

*** Figures in Columns C1-C3 are those in Column B adjusted for price inflation to 2002 but are distinguished from each other by the adjustments for direct medical cost inflation, as described below. The medical cost figures in C1 reflect the general increase in medical care prices (MCPI) applied to all medical costs, which implicitly assumes that the inpatient/outpatient mix of medical care for treatment of spina bifida was the same as that for the delivery of medical care in general in the United States. Our analysis demonstrated that inpatient care weighed more heavily in treatment of spina bifida than

care in general, however. The medical cost figures in C3 reflect the application of the inpatient component of the MCPI to inpatient costs and the "all other" medical care component of the MCPI to non-inpatient medical costs based on the mix of such care for those with spina bifida in our 1988 analysis. The corresponding figures in column C2, our "best" estimate, reflect the application of the same component inflation factors, but the weight of inpatient care in the mix is reduced by the general 17% shift away from inpatient care to other venues of care in the country between 1988 and 2002 (Levit et al, 2004). For all three of these columns (C1-C3), the change in various employee compensation indices (ECI) generated by the Bureau of Labor Statistics was applied to non-medical direct costs: the ECI for primary and secondary school teachers for special education costs, the ECI for public employees in the service sector for developmental services costs, and the general ECI for civilian workers for indirect costs. For indirect costs, a 1% annual productivity adjustment factor already included in estimates of future compensation was subtracted from the general ECI.

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