

Incidence of Disability Among Children 12 Months After Traumatic Brain Injury

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Traumatic brain injuries (TBIs) are the most common cause of death from trauma among children and adolescents¹ and one of the most common causes of acquired disability.² TBI surveillance systems have provided important aggregate information on the incidence of these injuries.³ Studies conducted in hospitals and rehabilitation centers have provided information on medical care⁴ and rehabilitation of patients with TBIs and their resultant impairments, focusing on those with more severe TBIs.⁵ However, population-based estimates of subsequent disability after pediatric TBIs are lacking. This population-based information is important to guide TBI prevention efforts and to ensure appropriate planning and delivery of services to children with TBIs who have special needs.

Although much of the focus in the literature has been on severe TBIs, concerns about the consequences of concussions and mild TBIs have recently increased in both the medical literature and the lay press.⁶ Available data indicate that mild TBIs are much more common than moderate or severe TBIs,^{7,8} and thus even if the consequences for most injured individuals are much less serious, mild TBIs have the potential to contribute a large share to the overall population TBI burden. In this study, we examined the burden of disability resulting from TBIs occurring among children younger than 18 years.

METHODS

The data presented here were gathered as part of a larger study on post-TBI disabilities among children residing in King County, Washington. We sought to identify all children younger than 18 years who had been treated for either a TBI or (for comparison purposes) an arm injury in each of 9 study hospitals; children were treated either in the emergency department or as inpatients and discharged. The 18 hospitals in King County with emergency departments serving children were

Objectives. We examined the burden of disability resulting from traumatic brain injuries (TBIs) among children younger than 18 years.

Methods. We derived our data from a cohort study of children residing in King County, Washington, who were treated in an emergency department for a TBI or for an arm injury during 2007–2008. Disabilities 12 months after injury were assessed according to need for specialized educational and community-based services and scores on standardized measures of adaptive functioning and social–community participation.

Results. The incidence of children receiving new services at 12 months was about 10-fold higher among those with a mild TBI than among those with a moderate or severe TBI. The population incidence of disability (defined according to scores below the norm means on the outcome measures included) was also consistently much larger (2.8-fold to 28-fold) for mild TBIs than for severe TBIs.

Conclusions. The burden of disability caused by TBIs among children is primarily accounted for by mild injuries. Efforts to prevent these injuries as well as to decrease levels of disability following TBIs are warranted. (*Am J Public Health*. 2012;102:2074–2079. doi:10.2105/AJPH.2012.300696)

classified into 3 strata: the regional children's hospital and the only level 1 trauma center, the county's 7 level 3 and level 4 trauma centers, and the 9 other non–trauma center hospitals. Both hospitals in the first stratum were included; 4 and 3 hospitals were randomly sampled from the second and third strata, respectively.

As described previously,⁹ study participants included parents of children and, for older age groups, the children themselves. Participants were randomly selected via computer-generated random numbers from the list of all eligible children treated between April 1, 2007, and September 30, 2008. Potential participants were contacted by letter and follow-up telephone call or, among those who had been admitted, in person.

Traumatic Brain Injury Definition and Severity

As recommended by the Centers for Disease Control and Prevention,¹⁰ a TBI was defined as a blunt or penetrating injury to the head and

documented in the medical record as having 1 or more of the following symptoms or signs: observed or reported decreased level of consciousness, amnesia, or objective neurological or neuropsychological abnormality or diagnosed intracranial lesion.

A mild TBI^{11,12} was defined as any period of observed or self-reported transient confusion, disorientation, or impaired consciousness as recorded in the patient's medical record; any period of observed or self-reported amnesia lasting less than 24 hours; or, in the case of very young children, observed signs of other neurological or other neuropsychological dysfunction such as posttraumatic seizures, irritability, lethargy, or vomiting following a head injury. Also, to be classified as having a mild TBI, patients had to have a worst Glasgow Coma Scale (GCS) score of 13 to 15 at the time of their first medical evaluation and a score of 15 at discharge from the emergency department or, if hospitalized, at 24 hours after injury.

A moderate TBI was defined according to a best motor GCS score at 24 hours postinjury

of 4 or 5 or a motor GCS score of 6 among those who did not meet the criteria for a mild TBI.¹² A severe TBI was defined as a best motor GCS score of 1 to 3 at 24 hours after injury. Because of the small number of patients with these injuries, moderate and severe TBIs were combined in our analyses.

Arm Injury Patients

As recommended by the Centers for Disease Control and Prevention,¹³ and consistent with previous studies on TBI,^{14–16} we used patients with isolated orthopedic arm injuries as comparison patients. Fifty controls were sought in each of 4 age groups (0–4, 5–9, 10–14, and 15–17 years) from the same study hospitals and during the same time period from which the TBI cases were sampled; comparisons were frequency matched to patients with mild TBIs with respect to gender.

Procedures

We conducted a baseline interview with one participating parent or guardian to ascertain children's functioning before their injury. In addition, adolescents aged 14 years or older who were able to participate completed baseline interviews as soon as possible after their injury. Follow-up questionnaires were completed 3 and 12 months after the date of the injury by the same respondents, either via phone or online. As shown previously, the responses obtained via these 2 modes of data collection were similar.⁹

Definition of Disability

We operationalized new disabilities in 2 ways. In the first approach, a new disability was evidenced by receipt of community resources among study participants who were not receiving such resources before their injury. These resources included services related to federal statutes intended to ensure that all children have equal access to education: special education for children with disabilities as outlined by the Individuals with Disabilities Education Act (104 Stat 1142), services for disadvantaged children as described in Chapter 1 or Title 1 of the Elementary and Secondary Education Act (79 Stat 27), and special accommodations arising from Section 504 of the Americans with Disabilities Act (104 Stat 327). Other special services included tutoring in the

community, rehabilitation therapies (occupational therapy, speech therapy, or physical therapy), and mental health services (e.g., counseling). Information on use of special school services was obtained from parents and confirmed by a review of school records.

In our second approach, we sought to identify those children who developed new functional and social-behavioral abnormalities, regardless of whether they were actually receiving services for these conditions. We conducted 3 parallel analyses with different abnormality thresholds that defined as disabled children who scored 1, 1.5, or 2 or more standard deviations below the mean of test norms for the Pediatric Quality of Life Inventory (PedsQL), the communication and self-care subscales of the Adaptive Behavior Assessment System (ABAS), and the Child and Adolescent Scale of Participation (CASP).

The PedsQL¹⁷ is a measure of health-related quality of life among children older than 24 months. The reliability and validity of the PedsQL as a measure of general physical and psychosocial health among children who have suffered TBIs and musculoskeletal trauma are well established.^{18–20} Total PedsQL scores range from 0 to 100, with a normative mean score of 80 (SD = 15). The ABAS (second edition; ABAS-II) is a multidimensional instrument that provides a comprehensive, norm-referenced assessment of adaptive skills.²¹ The ABAS-II includes 9 subscales; we used the communication and self-care subscales, for which the normative mean score is 10 (SD = 3). The CASP consists of 20 items measuring the involvement of children 5 years or older in various activities in the home, school, and community.²²

The Pediatric Symptom Checklist (PSC-17) is a measure of childhood emotional and behavioral problems. Children with a total score of 10 or above on the instrument are defined as having a disability. In the case of all of the measures included in our study, children whose preinjury score fell below the threshold and whose follow-up score exceeded the threshold were classified as having a new disability.

Medical Record Data

The principal investigator (Frederick P. Rivara) or a trained research nurse (blinded to

the baseline and outcome measures) used a standardized, online abstraction form to abstract data from medical charts. Preinjury comorbidities were identified from the medical record and comprised any cases of prior head trauma, prior surgery, or chronic illness from a predefined list that included developmental delay, seizures, prior TBI with loss of consciousness, hemiplegia or paraplegia, lung disease, diabetes, attention deficit hyperactivity disorder, depression, other mental health or behavioral problems, learning problems, and prior fractures.

Data Analysis

TBI incidence was calculated as described previously,³ and the same methods were used to determine the incidence of disability from TBIs. All incidence rate estimates and confidence limits accounted for the 2-stage sampling plan and stratification of hospitals. The estimates of disability incidence rates and confidence limits took into account the fact that study participants were not a random sample of injured children in King County because moderate and severe TBI cases were over-represented in the sample. Therefore, we used a resampling method to derive incidence and confidence interval (CI) estimates. We determined the number of children with TBIs at the study hospitals and imputed the disability status of children not recruited into the study. We used TBI severity and, when there were at least 20 known disability cases for a given measure, age as predictors in the imputation model.

We then drew a sample from these data, mimicking the sampling design used in the study, and counted the number of children with disabilities in the resulting data set; this procedure was repeated 4000 times. The confidence limits for the number of children with disabilities related to injuries were the 2.5th and 97.5th percentiles of that count across the 4000 replications. We converted these counts to rates by dividing by the corresponding number of child-years at risk determined from population estimates for King County according to age, gender, and calendar year.²³ We then examined the relationship between the disability measures and any new services at 12 months separately for TBIs and arm injuries.

RESULTS

A total of 436 patients with TBIs and 153 with arm injuries participated in the study; 62.2% of eligible TBI patients and 58.5% of eligible arm injury patients participated.²⁴ Enrollees were similar with respect to age and gender to those selected but not enrolled but were more likely to have a moderate or severe TBI and less likely to be seen at a lower level trauma center. Follow-up data were available for 90.8% and 92.4% of the children, respectively, at 12 months. The estimated incidence of nonfatal mild TBIs among children aged 2 to 17 years was 265.8 cases per 100 000 child-years (95% CI = 199.2, 329.4), and the incidence of nonfatal moderate or severe TBIs was 6.8 cases per 100 000 child-years (95% CI = 4.2, 9.5).

Receipt of Special Services

An estimated 222 children with TBIs of any severity in King County were receiving services at 12 months after their injury that they had not been receiving before their injury (Table 1). Overall, 61.6% of those with moderate or severe injuries received new services; among those with mild TBIs, 14.3% were receiving new services 12 months after their injury. By comparison, 8.3% of children with arm injuries were receiving new services.

Although the proportion of patients receiving special services was much higher among those with moderate or severe TBIs than among those with mild TBIs, the population burden of disability was mostly due to mild TBIs because of their much higher incidence. The population incidence rate of children receiving new services at 12 months was nearly 9-fold higher among those with mild TBIs than among those with moderate or severe TBIs (Table 1).

Despite the high incidence of TBIs in pre-school children, the incidence rate of disability after a mild TBI increased with age from 27.2 per 100 000 child-years among children aged 2 to 4 years to 66.2 among those aged 15 to 17 years at the time of their injury; the reason was that the percentage of mild TBI cases that were followed by a new disability increased with age from 8.2% to 22.0% in these groups. This pattern was not seen among those with moderate or severe injuries. The incidence of disability from TBIs varied according to gender; male patients, who had about a

TABLE 1—Incidence of New Services 12 Months After a Traumatic Brain Injury (TBI), by Age and Gender: Children Residing in King County, Washington, 2007–2008

	Estimated No. of Children Receiving New Service (% of Those Injured)		Estimated Disability Incidence Rate ^a (95% CI)	
	Mild TBI	Moderate/Severe TBI	Mild TBI	Moderate/Severe TBI
Total	200 (14.3)	22 (61.6)	37.9 (24.9, 52.4)	4.1 (2.1, 6.6)
Age group, y				
2–4	27 (8.2)	6 (100.0)	27.2 (5.0, 57.9)	5.9 (1.0, 12.0)
5–9	51 (14.9)	4 (100.0)	31.6 (13.4, 55.1)	2.4 (0.0, 5.6)
10–14	53 (12.7)	5 (50.0)	32.7 (14.6, 55.8)	3.0 (0.6, 6.2)
15–17	69 (22.0)	7 (44.3)	66.2 (28.3, 124.4)	6.6 (1.0, 15.3)
Gender				
Male	132 (14.1)	15 (59.2)	48.9 (30.5, 72.4)	5.4 (2.2, 9.3)
Female	68 (14.5)	7 (67.3)	26.5 (13.4, 40.7)	2.7 (0.8, 5.4)

Note. CI = confidence interval. Services included special education, 504 accommodations, Chapter 1/learning assistance programs, and occupational therapy/physical therapy/speech therapy/counseling/other.

^aRate of children receiving services per 100 000 child-years.

1.8-fold higher incidence of TBIs, had similarly higher rates of disability.

The types of special services children received are shown in Table 2. Special education, Chapter 1 or Title 1 programs, and accommodations under 504 plans are covered by federal statutes related to ensuring that all US children who require specialized instruction, are disadvantaged, or require accommodations as a result of a disability receive these services. The other services are community-based resources not specifically covered by federal statutes. In every instance, although the proportion of injured

children receiving new services was higher among those with moderate or severe TBIs than mild TBIs, the population incidence rate of new services was substantially higher among those with mild TBIs than those with moderate or severe TBIs. Only 3 children with arm injuries were receiving federally mandated new services 12 months after their injury.

Disabilities in Clinical and Social-Behavioral Domains

The numbers of children who scored greater than 1, 1.5, or 2 standard deviations below

TABLE 2—Receipt of Specific Services 12 Months After a Traumatic Brain Injury (TBI): Children Residing in King County, Washington, 2007–2008

	Estimated No. of Children Receiving Services (% of Those Injured)		Estimated Incidence Rate of Disability ^a (95% CI)	
	Mild TBI	Moderate/Severe TBI	Mild TBI	Moderate/Severe TBI
Services related to federal statutes				
Special education	31 (2.2)	6 (16.8)	5.8 (1.8, 11.3)	1.1 (0.2, 2.5)
Chapter 1/learning assistance	25 (1.8)	8 (22.4)	4.7 (0.8, 11.1)	1.6 (0.4, 3.4)
Plan 504 accommodations	24 (1.7)	2 (5.6)	4.5 (0.9, 10.0)	0.4 (0.0, 1.5)
Other services				
Occupational therapy/physical therapy/speech therapy	77 (5.5)	13 (36.4)	14.6 (7.2, 26.5)	2.4 (0.9, 4.4)
Tutoring	63 (4.5)	14 (39.2)	11.8 (5.8, 20.9)	2.7 (0.9, 5.1)
Any service	200 (14.3)	22 (61.6)	37.9 (24.9, 52.4)	4.1 (2.1, 6.6)

Note. CI = confidence interval.

^aRate of children receiving services per 100 000 child-years.

the mean norm on the measures of functioning are shown in Table 3. Again, the population incidence of disabilities as defined by these measures was consistently much larger for mild TBIs than for severe TBIs (ranging from 2.8-fold to 28-fold larger). At baseline, the percentages of children in the mild TBI group with disabilities, as measured by scores greater than 1, 1.5, or 2 standard deviations, ranged from 7.0% to 22.7%, 4.4% to 12.5%, and 1.7% to 7.0%, respectively. The incidence rates shown in Table 3 are those for new disabilities occurring after an injury.

Scores on these measures were correlated with one another, with correlation coefficients ranging from 0.32 to 0.71 (Table S1, available as a supplement to the online version of this article at <http://www.ajph.org>), indicating that a child who scored as impaired in one domain of functioning was more likely to be impaired in other domains as well. Although different measures are designed to assess different aspects of disability, this pattern of correlations provides evidence of the convergent validity of these measures of disability in our population. The percentage of children

who received new special services among those who scored 1 standard deviation or more below the norms on each measure varied but was never more than 38.5%, suggesting an unmet need for at least some children (Table 4).

These data also provide cross validation of our measures of disability because, in most instances, children with new disabilities identified on the standardized measures were more likely than those who fell within 1 standard deviation of the norm mean on each measure to be receiving new services as well. The exceptions, the ABAS self-care subscale and the CASP, may represent aspects of disability wherein the link to need for new services may not be as strong. None of the children with arm injuries who scored 1 standard deviation or higher received new special services.

DISCUSSION

Few population-based studies on the incidence of disability resulting from TBI have been conducted, and none to our knowledge have been conducted among children. We found that the overall population burden of

disability after a TBI is largely a consequence of mild TBIs rather than moderate or severe TBIs. Although the proportion of children with disabilities at 12 months was much greater among those with moderate or severe TBIs than among those with mild injuries, the higher incidence of mild TBIs resulted in their much greater contribution to the overall burden of disability. We also found that many children with disabilities as defined in this study did not receive special services.

We chose to define disability at 12 months after injury according to 2 approaches: receipt of new community services and a score beyond a certain threshold on standardized measures of functioning. We used the World Health Organization's International Classification of Functioning, Disability, and Health²⁵ in selecting the specific domains of functioning to be assessed in our study and the specific follow-up measures to be used.

An important aspect of the population burden of disability is the need for special services for those who are disabled. The services included in our definition require community resources from the school system as well as the health care and mental health care delivery

TABLE 3—Incidence of New Disability-Related Abnormalities 12 Months After a Traumatic Brain Injury (TBI), by Degree of Abnormality on Standardized Measures: Children Residing in King County, Washington, 2007–2008

Disability Measure	Age Range, Y	Estimated No. of Injured Children With New Disability (% of Those Injured)		Estimated Incidence Rate of New Disability ^a (95% CI)	
		Mild TBI	Moderate/Severe TBI	Mild TBI	Moderate/Severe TBI
PSC-17	2–17	114 (8.1)	8 (22.4)	21.5 (11.5, 33.7)	1.5 (0.4, 3.0)
Beyond 1 SD from norm					
PedsQL	2–17	120 (8.6)	11 (30.8)	22.8 (13.2, 36.1)	2.1 (0.8, 4.0)
ABAS II communication	0–17	71 (4.0)	6 (13.2)	12.0 (5.2, 20.3)	1.0 (0.2, 2.4)
ABAS II self-care	0–17	185 (10.5)	10 (22.0)	31.1 (19.1, 45.6)	1.6 (0.5, 3.0)
CASP	5–17	67 (6.2)	2 (6.7)	15.6 (7.2, 26.7)	0.4 (0.0, 1.6)
Beyond 1.5 SD from norm					
PedsQL	2–17	60 (4.3)	6 (16.8)	11.3 (5.3, 20.3)	1.1 (0.2, 2.7)
ABAS II communication	0–17	51 (2.9)	6 (13.2)	8.5 (3.2, 16.5)	1.0 (0.2, 2.2)
ABAS II self-care	0–17	143 (8.1)	3 (6.6)	24.0 (13.3, 39.1)	0.4 (0.0, 1.2)
CASP	5–17	38 (3.5)	2 (6.7)	8.8 (3.2, 16.8)	0.4 (0.0, 1.4)
Beyond 2 SD from norm					
PedsQL	2–17	31 (2.2)	4 (11.2)	5.8 (1.9, 14.3)	0.8 (0.0, 1.9)
ABAS II communication	0–17	20 (1.1)	6 (13.2)	3.4 (0.5, 8.3)	0.9 (0.2, 2.2)
ABAS II self-care	0–17	20 (1.1)	4 (8.8)	3.3 (0.5, 8.2)	0.7 (0.0, 2.0)
CASP	5–17	36 (3.4)	4 (13.5)	8.5 (2.7, 16.3)	0.9 (0.0, 2.1)

Note. ABAS = Adaptive Behavior Assessment System; CASP = Child and Adolescent Scale of Participation; CI = confidence interval; PedsQL = Pediatric Quality of Life Inventory; PSC-17 = Pediatric Symptom Checklist.

^aRate per 100 000 child-years.

TABLE 4—New Services Received 12 Months After a Traumatic Brain Injury (TBI), by Scores on Standardized Measures: Children Residing in King County, Washington, 2007–2008

Standardized Measure	TBI Group		Arm Injury Group	
	Total	Receiving Services, No. (%)	Total	Receiving Services, No. (%)
PedsQL				
< 1 SD from norm	287	44 (15.3)	102	9 (8.8)
≥ 1 SD from norm	26	10 (38.5)	6	0 (0.0)
ABAS communication				
< 1 SD from norm	300	53 (17.7)	99	9 (9.1)
≥ 1 SD from norm	14	1 (7.1)	9	0 (0.0)
ABAS self-care				
< 1 SD from norm	290	46 (15.9)	100	9 (9.0)
≥ 1 SD from norm	24	8 (33.3)	8	0 (0.0)
CASP				
< 1 SD from norm	257	46 (17.9)	87	9 (10.3)
≥ 1 SD from norm	16	3 (18.7)	2	0 (0.0)
PSC-17				
< 1 SD from norm	288	44 (15.3)	101	9 (8.9)
≥ 1 SD from norm	25	9 (36.0)	7	0 (0.0)

Note. ABAS = Adaptive Behavior Assessment System; CASP = Child and Adolescent Scale of Participation; PedsQL = Pediatric Quality of Life Inventory; PSC-17 = Pediatric Symptom Checklist.

systems. However, receipt of services depends on both need for services and access to those services, and access can vary according to many factors, including family socioeconomic status, family place of residence, and school policies. Our second (“statistical”) approach to measuring disability at least partially rectified the discrepancy between need for services and receipt of services by focusing on significant functional and social-behavioral effects of TBI.

The 2 methods we used provided complementary information in determining the burden of disability among children and adolescents created by TBIs. Services related to federal law are special education (individual educational programs), 504 accommodations, and Chapter 1 learning assistance. New mandated services were rare among our control group of children with arm injuries but were more frequent among children with TBIs, especially those with moderate or severe injuries. Nevertheless, the majority of children with moderate or severe TBIs did not receive such services. Somewhat more common were community-based tutoring, rehabilitative therapies, and counseling.

When we used the statistical definitions of performance on standardized measures covering quality of life, adaptive skills, participation in

age-appropriate activities, and behavioral-emotional problems, the incidence of disability was lower but still substantial. The Americans with Disabilities Act defines disability as “a physical or mental impairment that substantially limits one or more of the major life activities.”²⁶ We used the statistical cut points of 1, 1.5, and 2 standard deviations to show the full spectrum of children who may be disabled by TBIs.

Among children aged 3 to 8 years residing in Washington State, developmental delay is defined as scoring 2 standard deviations below the mean in 1 or more of 5 developmental areas or scoring 1.5 standard deviations below the mean in 2 or more areas.²⁷ Many children who met this criterion for one measure did not do so for other measures, indicating that different areas of functioning were affected in different children. Nevertheless, in every instance the population incidence of disability was again larger in the case of mild TBIs than in the case of moderate or severe TBIs.

Not all children with moderate or severe TBIs received special services at 12 months. In addition, not all children who scored above 2 standard deviations from the mean on the measures of functioning were receiving special services. This may indicate that these children have unmet needs (although we cannot

confirm this supposition). Previous studies have reported on unmet health needs of children 12 months after a TBI.²⁸

In recent years, much more attention has been paid to mild TBIs resulting from concussions, especially sports-related concussions.^{29–32} The symptoms and signs of these concussions, as well as their possible longer term consequences, had often previously been overlooked or discounted, thereby leading to underestimation of the population incidence of TBIs.

Our participants all sought care at hospital emergency departments; those with concussive symptoms who either did not report them or did not seek care in an emergency department would thus have escaped detection. Recruitment of patients into this study occurred before the implementation of a mandatory reporting law in Washington State for sports-related concussions. Thus, the population burden of disabilities after mild TBIs may be larger than we have estimated. The incidence of disabilities after mild TBIs increased with age, a relationship not observed among those with moderate or severe injuries. This pattern is rather different from the pattern of variation in TBI incidence with age, which is U-shaped.

Limitations

A number of limitations must be considered when interpreting our results. Because patients with less severe TBIs were less likely to participate in the study, our estimates of disability may be biased. Although we used medical reports, computed tomography scans, and parents’ reports to classify TBI severity, injury severity within groups (mild, moderate or severe) may not have been homogeneous, and this heterogeneity may account for some of the variation in who received services.

In addition, although all patients were from King County, they attended many different schools in a variety of districts that may differ in the degree to which the needs of children with disabilities are met. Some children with a mild TBI may be receiving new services after injury for preexistent conditions rather than for disabilities resulting from their TBI, potentially inflating our estimates of disabilities due to TBIs. We did not have information on the reasons why our participants received new services. Although preinjury disabilities were not included in our estimates of new disabilities, some

children may qualify for special services for reasons unrelated to their injuries.

We did not attempt to collect a population sample of children with arm injuries, and thus we could not generate incidence rates for disabilities due to arm injuries. However, 8.3% of children with arm injuries were receiving new services at 12 months, compared with 14.3% of those with mild TBIs. Finally, this study focused on only one area of the country. Regional differences in the availability of services and awareness of injuries, especially of mild injuries, may result in different rates of disability and receipt of services.

Conclusions

We found that the population burden of disability after a TBI among children residing in King County, Washington, was primarily accounted for by mild TBIs. Efforts to prevent these injuries, to identify those children with mild TBIs who are at the highest risk for becoming disabled, and to decrease levels of postinjury disability are warranted. ■

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Contributors

F. P. Rivara wrote the first draft of the article. The analysis was led by T. D. Koepsell, J. Wang, and N. Temkin. All of the authors contributed to the conceptualization of the study, interpretation of the findings, and review and editing of the article.

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Human Participant Protection

This study was approved by the human subject committees of all of the participating institutions. Written informed consent was obtained from all parents, and written assent was obtained from children 14 years or older.

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