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# Examining the characteristics of children with spina bifida in a population-based surveillance system and a clinic-based patient registry

By

Jaynia Angela Anderson

Degree to be awarded: Master of Public Health

Epidemiology

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# Examining the characteristics of children with spina bifida in a population-based surveillance system and a clinic-based patient registry

By

Jaynia Angela Anderson

Bachelor of Science
University of California Santa Barbara
2008

Faculty Thesis Advisor: Penelope P. Howards, PhD, MS
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An abstract of
A thesis submitted to the Faculty of the
Rollins School of Public Health of Emory University
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## Abstract

Examining the characteristics of children with spina bifida in a population-based surveillance system and a clinic-based patient registry

By Jaynia Angela Anderson

**Background:** Spina bifida substantially contributes to perinatal mortality and lifelong disability. Population-based surveillance systems monitor birth defect trends, risk factors, and effectiveness of prevention programs. Clinic-based patient registries provide data for advancing knowledge in the understanding of disease progression and management.

**Methods:** Demographic and clinical characteristics were described for 3,685 children with spina bifida included in a population-based surveillance system and 1,598 children with spina bifida included in a clinic-based patient registry. The distributions of race/ethnicity among the two systems were compared with the respective underlying statewide and metropolitan area populations. The distributions of spina bifida subtypes by race/ethnicity were also described.

**Results:** The race/ethnicity distributions of both systems were significantly different from their respective underlying populations, with an under-representation of NH black children. Most children in both systems had the myelomeningocele or related subtype and more than half had hydrocephalus. In both systems, the distribution of spina bifida subtype was similar among NH white and NH black children but different among Hispanic children.

**Conclusions:** Population-based surveillance systems assist in quantitatively evaluating the burden of spina bifida in the population, and clinic-based patient registries are useful in understanding the clinical characteristics of spina bifida patients. Similar overall patterns are seen in both catchment systems and the two systems differ from the underlying populations. The population-based surveillance system differ because of the differing burden of disease across race/ethnicity groups; and the patient registry might differ because of issues related to access to care and utilization of care by different race/ethnicity groups. However, there was insufficient data available to determine the cause of the observed differences.

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## Background/Literature Review

### *Neural Tube Defects*

Development and closure of the neural tube normally occurs within 28 days after conception, a time in which many women are unaware of their pregnancy (1-3). The neural tube is the primordium of the entire central nervous system- the brain and spinal cord. Development occurs via the neurulation process, involving a series of coordinated morphologic events in which the ends of a sheet of tissue fold together to form a tube (1, 4). Neural tube defects occur when the neural tube fails to properly fuse during embryogenesis leaving a gap in which nerves, tissues, fluid and the spinal cord are exposed, leading to severe neurological and/or developmental disorders (4-6). Neural tube defects can occur at the cranial or spinal levels and make up a group of severe birth defects including anencephaly, craniorachischisis, spina bifida, encephalocele, and iniencephaly; of which spina bifida and anencephaly are the most common (1, 6). Neural tube defects substantially contribute to perinatal mortality and lifelong disability in children who survive (7, 8).

### *Spina Bifida*

Spina bifida refers to a group of defects that occur when there is a herniation of the meninges or spinal cord tissue through a bony defect of spine closure. This results in incomplete development of the spinal cord or the meninges (1). The different subtypes of spina bifida are based on the location and type of lesion (6).

The most common and extensively studied subtype is Myelomeningocele, characterized by cystic herniation of the spinal cord, meninges, and cerebrospinal fluid,

covered by a sac-like membrane. Myelomeningocele may be located anywhere along the spine but is most commonly located in the lumbosacral region (6, 9). Less common subtypes include: myelocele, meningocele, myelocystocele, and lipomeningomyelocele. Myelocele is similar to myelomeningocele, but lacks a membranous sac and is typically located at the bottom of the spinal canal. Meningocele involves herniated meninges and cerebrospinal fluid, and not the spinal cord. Myelocystocele is a cystic lesion of the spinal cord central canal and herniation, and can occur anywhere on spine, but most instances occur in the sacral region (6, 9). Myelomeningocele, myelocele, and meningocele are thought to have related etiologies (9). Lipomeningomyelocele is thought to have a different etiology and is defined by the presence of excessive fatty tissue connected to the spinal cord or filum terminale, usually located in the lumbosacral region (6, 9). Spina bifida occulta is the mildest type of spina bifida and is sometimes referred to as “hidden” spina bifida because there is no opening or sac, and it is often asymptomatic (10). This subtype is not included in estimates of spina bifida; it usually does not cause disability and may involve different causal factors (6, 10).

The majority of spina bifida lesions are open, in which the neural tissue is exposed to the environment or covered only by a membrane; myelomeningocele, myelocele, and meningocele are classified as open lesions. Closed lesions are covered by normal skin; lipomeningomyelocele is classified as a closed lesion (6, 10). It has been postulated that open defects occur during primary neurulation, in contrast to closed defects which are thought to occur postneurulation (6). Classification is also based on the highest level of the location of the lesion on the spine: cervical, thoracic, lumbar, or

sacral. The higher the occurrence of the lesion, typically, the more severe the defect (6, 10).

Hydrocephalus is an associated malformation of the nervous system (11), and it occurs in approximately 85% of infants with myelomeningocele and in some children with closed lesions (12). It is a condition in which cerebrospinal fluid accumulates abnormally, causing dilation of the ventricles and increased intracranial pressure (13). In some cases hydrocephalus is the result of Arnold Chiari type II malformation, in which the cerebellar portion of the brain protrudes into the spinal canal, or aqueductal stenosis, in which the flow of cerebrospinal fluid is blocked (14, 15). The majority of those with hydrocephalus require surgical treatment, with a ventriculoperitoneal shunt placement within the first week of life (6, 16). The shunt allows drainage of cerebrospinal fluid from the cerebral ventricles into the peritoneal space through a catheter (6). A previous study found that 97% of those with a lesion in the thoracic level, 88% of those with a lumbar level lesion, and less than 70% of those with a sacral level lesion require shunt placement (11, 16).

*Prevalence and Survival*

The estimated national prevalence of spina bifida in the United States is 3.5 per 10,000 live births (17, 18). National birth prevalence estimates by race/ethnicity are 3.4 per 10,000 live births for non-Hispanic (NH) whites, 2.9 per 10,000 live births for NH blacks, 4.2 per 10,000 live births for Hispanics (19). Current prevalence estimates of spina bifida among children and adolescents ages 0 to 19 in 10 regions in the United States were estimated to be 3.1 per 10,000 children for NH whites, 1.9 per 10,000

children for NH blacks, 3.6 per 10,000 children for Hispanics, and 1.8 per 10,000 children for other races (20). It is estimated that there are 1,460 birth prevalent cases of spina bifida annually in the United States (12, 17, 18).

Prior to 1960, the one year survival rate for all subtypes of spina bifida was 55% (21). With advances in medical treatment, more infants born with spina bifida are surviving longer and the majority of individuals born with spina bifida will survive if given the appropriate treatment (5). A 2006 study reported a one-year survival rate of 91.2% for a cohort of live births from 1995-2001 (18). Similar results were seen in a 2010 study, which reported that the one-year survival rate increased from 87.1% in 1983 to 93.6% in 2002 among 9 state population-based surveillance systems and estimated the 20-year survival rate to be 85.2% for the years 1983-2003 of selected states among these 9 systems (20).

*Declines in Birth Prevalence: Folic Acid Fortification and Other Factors*

Neural tube defects occur worldwide, however the prevalence varies by race/ethnicity within geographic regions and time periods (5, 7). In recent decades, the dramatic declines in children born with spina bifida can largely be attributed to increased maternal folate levels (7, 22). Periconceptional folic acid supplementation can significantly reduce a woman's risk of having a child with a neural tube defect (5). This finding was a significant public health breakthrough in the prevention of neural tube defects (5, 7, 23). Maternal intake of folic acid from 3 months before pregnancy through the first month of pregnancy has been associated with lower rates of spina bifida among

pregnant women compared to those who initiated intake of folic acid during or after the first month of pregnancy (22).

Therefore, it has been recommended that all women of childbearing age ingest 400 μg (0.4 mg) of folate daily, which may decrease the occurrence of neural tube defects by up to 70% (24). However, despite numerous efforts, there has been little success in increasing the proportion of reproductive aged women who consistently consume folic acid containing supplements, limiting the impact of this potential intervention (25-27).

In contrast, a 30-50% reduction in the prevalence of neural tube defects has been observed in areas with mandatory folic acid food fortification programs (7, 19, 22-24, 28-31). In the United States, folic acid fortification of all enriched cereal grains became mandatory in January 1998; this resulted in significant increases in blood folate levels in women of childbearing age coinciding with a decline in neural tube defect affected births (7). It was found that there was an approximate 36% reduction in the occurrence of spina bifida in Hispanics, a 34% reduction in NH whites, and a 19% reduction in NH blacks (19). Surveillance data strongly points to falling overall NTD rates in most developed countries in the past 3 decades where fortification programs have been implemented (23).

While a decline has been seen, cases of spina bifida are still occurring, possibly due to the existence of certain subpopulations that require higher doses of folic acid or are not adequately reached by currently fortified foods (32-35). Some evidence has suggested that even though prenatal folic acid does not prevent all spina bifida affected births, it may lessen the severity of the spina bifida (18). However, spina bifida also continues to persist because many cases are not preventable by folic acid and instead have other causes such as certain medications (36, 37).

Other factors contributing to declines in neural tube defects include prenatal screening and elective pregnancy terminations (38, 39), increased understanding of nutritional risk factors for neural tube defects (40), and some prevention programs encouraging vitamin supplementation (41, 42). Prenatal diagnosis of neural tube defects is done typically between 15 and 20 weeks gestation of pregnancy through α-fetoprotein screening and fetal ultrasonography to provide time for decision-making (12). Elective termination rates following a prenatal diagnosis of a neural tube defect have been shown to vary temporally and regionally (38).

*Epidemiology and Risk Factors*

The etiology of neural tube defects and spina bifida remains poorly understood; it is believed that both genetic and environmental factors contribute (4). Previous studies have suggested that there are some genetic risk factors, finding that the occurrence of neural tube defects among first and second degree relatives of those with neural tube defects to be meaningfully higher relative to the general population (43, 44). One study found an increased risk of 2-5% for recurrence in siblings of patients with neural tube defects relative to the general population (43). Factors known or highly suspected of increasing the risk of neural tube defects include female infant sex (45), family history of neural tube defects (5), maternal Hispanic ethnicity (46, 47), obesity (48, 49), folate status (22), pre-gestational diabetes and gestational diabetes (50), anticonvulsant use (51), and hot tub or sauna use (52). In the United States higher rates of neural tube defects are observed among Hispanics than NH whites and NH blacks (9, 53). Based upon geographic and temporal variability, it has been suggested that there may be interactions

between ethnic background and environmental factors among Hispanics (54). A study by Agopian, et al., found that as of December 2007 known neural tube defect risk factors accounted for approximately 28% of spina bifida risk after adjusting for the overlap in the occurrence of risk factors (52). The factors found to be associated with the greatest proportion of cases included maternal Hispanic ethnicity, obesity, low dietary folate intake, female infant sex, and lack of folic acid supplementation (52). Additional risk factors have been identified in more recent epidemiological studies including: opioid use (37), antiepileptic medications (36, 55), maternal smoking (56), and maternal caffeine consumption (57).

*Healthcare Needs and Living with Spina Bifida*

Children born with spina bifida require both immediate and long-term medical, surgical, and other related interventions (20, 58). With developments in medical technology and changing attitudes toward disability, the experience of living with spina bifida has greatly improved since the 1960s (21, 59). In the 1940s before the introduction of antibiotics, most infants born with myelomeningocele died from meningitis or hydrocephalus. During this time, many infants were not surgically treated, and many who were treated developed complications such as infections and mental retardation (60). Due to the poor prognosis of spina bifida, some providers in the United States and United Kingdom developed criteria for selective treatment of children affected by spina bifida; and those that were not selected were allowed to die (60, 61). The development of shunts in the 1950s revolutionized the treatment of myelomeningocele; however, those who survived meningitis and hydrocephalus had renal complications, which became the

leading cause of death for individuals with myelomeningocele in the 1970s (21). Additionally, during the 1970s and 1980s, it was not uncommon for children with spina bifida to be hospitalized for weeks at a time for orthopedic surgery or other treatment (60).

In 1985, the United States Congress adopted a set of Baby Doe rules as amendments to the Child Abuse and Neglect Funding Requirements for States which mandated provision of life-sustaining medical treatment to most seriously ill infants (60). These amendments were adopted on the basis of the birth of a girl who had spina bifida and hydrocephalus, Baby Jane Doe, whose parents declined surgical treatment (60). Since then almost all newborns with spina bifida are treated, and by the mid-1980s, most children living with myelomeningocele could achieve independent mobility and continence (21, 60). Additionally, the development and innovation of the ventricular shunt to treat hydrocephalus and clean intermittent catheterization increased longevity and quality of life (60).

The clinical effects and complexity and severity of spina bifida are related to the location and size of the defect; the presence of hydrocephalus, brain abnormalities and other neurologic and orthopedic conditions (12); and the presence of other co-morbidities (5, 6). Immediate care includes surgical closure of an open lesion within 72 hours after birth to decrease the risk of central nervous system infection (12). The treatment of other conditions associated with spina bifida following the repair of the spinal defect may range from simple observation to extended surgical procedures (62).

Functional defects of the urogenital and lower intestinal tract are associated with defects at all levels. Motor and sensory deficits and structural abnormalities in lower

extremities are associated more with thoracic and higher lumbar lesions than lower lumbar or sacral regions (12). The presence of hydrocephalus necessitates ventricular shunt placement and regular monitoring in most cases. Hydrocephalus is also associated with significant learning problems and decreased cognitive functioning (12, 63)*;* shunt-related neurological conditions are common, and side effects such as pain are costly and affect quality of life (63). Most children with spina bifida have abnormal bowel function because recto-anal function is innervated by sacral nerves, and some children have decreased gastrointestinal motility thought to be secondary to abnormal migration of nerve cells into the gut (60).

Other comorbid conditions include learning disabilities, problems with attention and executive function, dysfunction of upper extremities, strabismus, seizures, and increased risk of developing latex allergies (12, 64, 65). Functional complications can include limitation of movement and ambulation, scoliosis, joint instability, fractures, bowel and bladder dysfunction, altered growth including precocious puberty, and obesity (12, 59, 66). Additionally, there are physical and psychological consequences, such as impaired mobility and independence, and having an altered appearance, which can be barriers to social integration (12).

Optimal care of an infant or child with spina bifida is best provided by a multispecialty team to provide comprehensive and coordinated care and support to the child and family (12). A multidisciplinary team typically includes a primary care physician; a clinical nurse specialist or nurse practitioner; pediatric specialists in neurosurgery, orthopedics, urology, and developmental pediatrics; physical therapists; orthotists; psychologists; social workers; and health education professionals (12).

Spina bifida not only affects the child but also the family; the challenges of having a child with spina bifida are not only coping with psychological and economic effects but also learning the surveillance and management skills necessary to ensure the child's physical and psychological well-being (67). The knowledge and skills necessary for long-term management of spina bifida include: pathophysiology of spina bifida, shunt care, continuous intermittent catheterization, bowel management, skin care, medication administration, and the use and maintenance of assistive devices. In addition, children with spina bifida need access to support and resources necessary for obtaining health-related accommodations needed for school, work, and community living (67).

Chronic conditions of the nervous system, musculoskeletal system, and genitourinary system, as well as pain, and sleep disturbance account for a large portion of the health care needs of children and adults with spina bifida. These conditions also require the greatest health-related expenditure (63).

While the health outcomes of children with spina bifida vary, all children with spina bifida are likely have extensive health care needs and costs (65). The average lifetime medical cost to a person with spina bifida is more than $635,000 (12). Children with spina bifida have greater than the average medical care utilization and incur greater costs compared with children with other special health care needs. The medical costs of children with spina bifida ages 1-17 years are estimated to be 13 times the costs for children not affected by spina bifida (58). The average medical expenditures in 2002-2003 during the first year of life for infants with spina bifida were approximately $50,000 with inpatient admissions costs due to infant surgeries accounting for the largest portion.

After infancy, average annual expenditures ranged from $15,000 to $16,000 for different age groups (58).

*Specialty Clinics*

Children with spina bifida have complex health care needs with many requiring the care of specialists who can address issues such as hydrocephalus, neurogenic bowel and bladder issues, mobility issues, and learning disabilities. Generalists are also needed to address health promotion, such as nutrition and exercise along with an integrated system to deliver, align, and inform all providers involved in care (60). Care is typically received from various medical and surgical subspecialists including pediatricians, neurosurgeons, orthopedic surgeons, urologists, and rehabilitation physicians (65). The long-term results and outcome of care depends greatly on the management of associated conditions. A child with spina bifida that has good health habits and a supportive family and caregiver will generally have a good prognosis for a normal life span (62).

Spina bifida clinics began to emerge in the 1970s and were established as places where children could receive continuous coordinated care from multi-disciplinary teams (21). These multi-disciplinary clinics can rapidly and effectively communicate information among caregivers and to the patient's local community. In addition, they are convenient for the patient and physicians (68). During the 1960s and 1970s, as the prevalence of polio decreased, many clinics that were originally established to treat children with polio were converted to provide care for children with spina bifida. Over time, these clinics added other providers in addition to orthopedists, physical therapists and neurologists. During the 1970s and 1980s, multi-disciplinary clinics providing

outpatient care for children with spina bifida were found in almost every state in the United States (60).

Currently, the multi-disciplinary clinic remains the preferred model of health care delivery to children with spina bifida (69). Consistent and long-term follow-up by a multidisciplinary team is essential for a good prognosis for a normal life span (62). A study done by Kaufman et al (1994) outlined the consequences of disbanding a spina bifida clinic in St. Louis, Missouri. After the disbandment, more than half of the patients failed to receive regular or specialty care resulting in more hospitalizations for preventable conditions in patients from the closed programs compared with patients continuing to receive multidisciplinary care at another clinic (68).

*Birth Defects Surveillance*

Broad objectives of state birth defects surveillance programs include estimating baseline birth defects prevalence, monitoring the relation of trends to environmental factors, performing cluster investigations, and providing the basis for etiologic studies (70). Surveillance is also useful for the purposes of planning and prevention, educational services, social services, and healthcare and human services (70, 71). The benefits of surveillance include identifying children in need of services, evaluating service utilization, and planning the location of services for particular conditions in areas of highest need (70).

Several state surveillance programs have been key in conducting etiologic research on risk and prevention factors of birth defects (4, 5, 7, 23, 52, 72, 73). The ability to estimate birth defects prevalence and the numbers of children surviving beyond

infancy allow for estimation of future service needs. The surveillance data allow for prediction of the demand for accessible resources and service providers including interdisciplinary clinics and social and educational services for children born with birth defects (20, 70, 71).

*Disease-specific Registries*

Knowledge regarding health status and long-term health outcomes of people with spina bifida is limited. As the number of individuals living with spina bifida increases due to longer life expectancy, it is increasingly important to understand the evolution and management of their health issues over the lifespan (74). Research on health-related outcomes in adults with spina bifida shows the importance of acquiring knowledge and self-management skills necessary for health maintenance and spina bifida condition stability. Problems in self-management, can result in serious, long-term consequences that can be life limiting (67).

Patient registries have the potential to be powerful tools for advancing the understanding of disease progression and management, especially for rare diseases such as spina bifida. These disease-specific registries provide systematically collected data for observational studies to follow patterns in disease diagnosis, treatment, and outcomes over time, in existing practice settings (75, 76). In addition, maintaining aggregated national demographic and health outcomes data on children and youth that have rare illnesses with special health care needs that have rare illnesses is critical for identifying and understanding health disparities (77). More recently, the use of registries have evolved to include evaluation of clinical effectiveness and safety of new therapies and

measuring quality of care (78). The registries provide data related to risk factors and exposures that are more difficult to obtain from randomized clinical trials (75).

However, the validity of registry data analysis is threatened by similar biases as observational studies. Selection bias is a major concern; the extent to which a given registry population represents the broader population is unknown (79). Patients included in a registry might differ due to disease severity (79). The complexities and functionality differ between the spina bifida subtype, those with the myelomeningocele subtype typically have lower mobility and social function compared with children with lipomyelomeningocele and may require more intensive care (80). Children affected by spina bifida who are not included in the registry may not be able to or may choose not to access health care (81). In addition, loss to follow-up may also be of concern when attempting to follow disease progression among individuals. There may be loss to follow-up among healthier individuals, or it may be too great of a burden to continue to participate for the sicker individuals (81). Information bias is also of concern, if measurements are systematically different between groups or clinics, there is a threat to validity. Additionally confounding is of concern because of potentially unmeasured variables. When addressing a research question not previously anticipated, information on potential confounders might not have been considered for initial inclusion in the registry. An additional hazard is in the interpretation of observational data, as with all studies, in which causality may be inferred but cannot be proven (75).

These limitations and concerns should be considered when analyzing and interpreting registry data. While registry data is very useful and can provide essential information on diseases, especially rare diseases, the potential for generalizability is

limited. This limitation is an extremely important factor to consider when examining disease progression and management among specific populations such as the National Spina Bifida Patient Registry.

The results from clinical research have been important in advancing the understanding and management of many conditions over the past decades. For example, cystic fibrosis has been extensively researched through the use of registries (76). The availability of disease registries to evaluate outcomes has greatly benefited cystic fibrosis care by serving as an important quality improvement engine. Findings from the Cystic Fibrosis Foundation registry has been instrumental in helping to determine and promote optimal care processes that lead to better disease outcomes for patients with cystic fibrosis (75). The cystic fibrosis system provides an example of taking advantage of existing knowledge to improve health outcome of children with chronic diseases (78). Based on the successful experiences of the cystic fibrosis registry system, the National Spina Association Professional Advisory Council proposed the establishment of the National Spina Bifida Patient Registry (74).

*Summary/Conclusion*

The purpose of this study is to describe the demographic and clinical characteristics of children born with spina bifida included in state-based, population-based surveillance systems in 9 regions of United States. And to describe the demographic and clinical characteristics of children with spina bifida included in a national clinic-based registry that are receiving care at 19 multidisciplinary clinic sites in different regions of the United States. The objectives are to assess the sex and

race/ethnicity distributions within the two separate ascertainment systems and to compare these distributions to the respective underlying populations of children born in the same years. A third objective is to examine the distribution of spina bifida subtypes and sub-phenotypes within the two separate systems, and their distributions by race/ethnicity.

Results of these analyses will identify key characteristics of children with spina bifida included in a population-based surveillance system that is assumed to capture all births and of children that are included in a clinic-based registry system that for multidisciplinary spina bifida clinics. These characteristics of children in the registry can help inform the potential selection bias of clinic-based ascertainment and can provide data for future quantitative studies examining this bias. The percentage of the population that attends clinics is unknown, and the health status of those not attending clinics might differ from those obtaining care in other settings (43). No current literature has documented the characteristics of two spina bifida populations ascertained differently in multiple geographic regions. With continuing improved survival, the burden on health care, especially for multidisciplinary clinics will increase. Information collected and drawn from a population-based system and a clinic-based system will be useful in improving the care and quality of life of children with spina bifida.

**Introduction**

Spina bifida refers to a group of neural tube defects that occurs when there is a herniation of the meninges or spinal cord tissue through a bony defect of spine closure. This results in incomplete development of the spinal cord or the meninges (1). The different subtypes of spina bifida (myelomeningocele, myelocele, meningocele, myelocystocele, and lipomeningomyelocele), and their severity are based on the location and type of lesion (6). Hydrocephalus, a condition in which cerebrospinal fluid accumulates abnormally causing increased intracranial pressure (13) occurs in approximately 85% of infants with myelomeningocele and in some children with closed lesions (12). The majority of those with hydrocephalus require surgical treatment, with a ventricular shunt placement within the first week of life (6, 16). Children born with spina bifida require immediate and long-term medical, surgical, and other related interventions (20, 58). The type of medical care varies across spina bifida subtypes and associated conditions (6, 82).

Neural tube defects occur worldwide, however the prevalence varies by race/ethnicity and within a given geographic location and time period, with the highest prevalence in the U.S. occurring among Hispanics (5, 7, 19). With improved medical treatment and care, the survival of those born with spina bifida has improved. A current estimate of one-year survival based on data from 10 population-based surveillance systems is 93.6%. For population-based surveillance systems with longer-term data available, the 20-year survival rate is estimated at 85.2% (20).

The clinical effects, complexity, and severity of spina bifida are related to the location and size of the defect, as well as the presence of hydrocephalus, brain

abnormalities, and other neurologic and orthopedic conditions (12). Immediate care includes surgical closure of an open lesion within 72 hours after birth to decrease the risk of central nervous system infection (12). The treatment of other conditions associated with spina bifida following the repair of the defect may range from simple observation to extended surgical procedures (62). Currently, the multi-disciplinary clinic remains the preferred model of health care delivery to children with spina bifida (69). As the number of individuals living with spina bifida increases due to longer life expectancy it is increasingly important to understand the evolution and management of their health issues over the lifespan (74).

Population-based surveillance systems and clinic-based disease registries generally have different purposes and goals. Patient registries provide data for observational studies in which information is systematically collected to follow patterns in disease diagnosis, treatment, and outcomes over time, in existing practice settings (75, 76). Current birth defects surveillance systems monitor birth defects trends, assess risk factors, and evaluate effectiveness of prevention programs. Several state surveillance programs have been key in conducting etiologic research on risk and prevention factors of birth defects (4, 5, 7, 23, 52, 72, 73).

This study aims to describe the demographic and clinical characteristics of children born with spina bifida included in a state population-based surveillance system in 9 regions of the United States and to describe the demographic and clinical characteristics of children with spina bifida included in a national clinic-based registry who are receiving care at 19 multidisciplinary clinic sites in different regions of the United States. We sought to assess the sex and race/ethnicity distributions within the two

separate ascertainment systems, to compare these distributions to the respective underlying populations of children born in the same years, and to examine the distribution of spina bifida subtypes and sub-phenotypes within the two separate systems.

## Methods

### *National Birth Defects Prevention Network*

The purpose of the National Birth Defects Prevention Network (NBDPN) is to conduct birth defects surveillance, research, and prevention. The network was established in 1997 to assess the impact of birth defects on children, families, and healthcare; identify factors that can be used to develop primary prevention; and assist families and their healthcare providers in secondary disabilities prevention (17). Detailed methods for data collection have been published elsewhere (83). Currently, the NBDPN collects state level data on the occurrence of 45 categories of major birth defects from 41 population-based birth surveillance systems (2013 NBDPN Annual report and Data Directory). Sources of data include medical records information and hospital administrative data.

All state-based programs reporting data to the NBDPN were invited to participate in this study. In order to participate, each surveillance system had to provide de-identified individual level data on all live-born infants with spina bifida between the years 1999-2007. Participating states for this analysis include: Arizona, Florida, Georgia, Illinois, Michigan, Nebraska, New York, North Carolina, and Texas. All systems provided statewide data except for Georgia, which provided data from five metropolitan Atlanta counties only, and New York, which provided data from all counties except those of metropolitan New York City. All states submitted data for the birth years1999-2007

except for North Carolina, which submitted data restricted to 2003-2007. The programs provided select maternal and infant demographic data for spina bifida cases, diagnostic codes for all major birth defects using either International Classification of Diseases, 9th Revision, Clinical Modification [ICD-9-CM] or Centers for Disease Control and Prevention/British Pediatric Association Classification of Diseases [CDC/BPA]), and counts of live births in their catchment areas for births occurring between 1999-2007. For race/ethnicity assessment, infants were classified based on maternal race/ethnicity because infant race/ethnicity was not available.

*National Spina Bifida Patient Registry*

The National Spina Bifida Patient Registry (NSBPR) is a clinic-based registry system that includes persons of all ages with spina bifida among those who have visited a spina bifida clinic participating in the registry, been invited to participate, and have consented to enroll (74). The Spina Bifida Association's Professional Advisory Council advocated for the establishment of the registry in 2009, based on assessments of spina bifida clinics. The Centers for Disease Control and Prevention (CDC) funds and facilitates the operations of the registry, serves as the Data Management Center ensuring data quality, and guides analysis and interpretation of the data in collaboration with the principal investigators. The goals of the registry include the following: to provide infrastructure to support spina bifida clinical research, to promote a systematic approach to describe the spina bifida clinic population, and to document and improve the quality of spina bifida clinical care. There are 19 clinics participating in data collection for the

registry and approximately 3,500 persons with spina bifida, ages 0-71 enrolled. Clinic eligibility for participation in the registry has been published elsewhere (74).

Clinic sites located in the states of Alabama, California, Colorado, Connecticut, Illinois, Indiana, Massachusetts, Michigan, North Carolina, Ohio, Oregon, Pennsylvania, Utah, Washington, and Wisconsin participate in the registry, with multiple participating clinics in some states. Sources of patient data include medical records from which diagnoses information is obtained, and patient interviews from which information on school level, continence, and mechanisms that support mobility are obtained. These data are entered into a web-based Spina Bifida-Electronic Medical Record (SB-EMR) system. These records are reviewed for accuracy and quality and are managed at the CDC by the NSBPR Data Management Center (74). Selected de-identified demographic and clinical characteristics of patients with spina bifida born in the years 1999-2007 were provided by the NSBPR Data Management Center for this study. Information on cervical lesion levels is not collected, and shunt placement is used as a proxy for evidence of hydrocephalus in the NSBPR.

*Underlying Populations*

Statewide NBDPN surveillance programs provided live births from 1999-2007; these data were used to represent the underlying population for these systems. While the geographical catchment area for clinical data in the NSBPR is unclear, the underlying population birth data were estimated based on publicly available data from the National Center for Health Statistics (NCHS). The data are bridged-race population estimates produced by the United States Census Bureau in collaboration with the NCHS (84). The

data include singleton live births from 1999-2007 in all counties in the metropolitan areas or states of the registry sites. Because the catchment area was unclear for the clinics participating in NSBPR, we estimated the underlying population at both the metropolitan statistical area level and statewide level and compared the clinic population to both.

*Statistical Methods*

We described child sex, race/ethnicity, vital status, spina bifida subtype, level of lesion, presence of hydrocephalus, and presence of other birth defects using frequency and summary statistics for the NBDPN overall and the NSBPR overall, as well as for the individual states and clinic sites within each system. For the NBDPN, the crude birth prevalence was estimated by sex and by race/ethnicity category by dividing the number of spina bifida cases by the total births, obtained from the underlying populations.

We report differences among the individual states or clinic sites and their reference populations using inferential statistics to assess the differences in sex and race/ethnicity distributions of children in the NBDPN, the NSBPR, and the statewide and metropolitan area reference populations using Pearson's chi-square goodness of fit tests. Spina bifida subtype, presence of hydrocephalus, and sex of cases across race/ethnicity categories were assessed for the NBDPN and the NSBPR. Myelomeningocele, meningocele, and myelocele subtype categories were combined because the etiologies of these subtypes are thought to be similar (6) and limited detail on subtype was available from some states in the data provided.

## Results

*National Birth Defects Prevention Network*

There are 3,685 eligible fetuses and infants with spina bifida among 11,483,204 total live births in the NBDPN study regions for birth years 1999-2007, yielding a crude birth prevalence of 3.2 cases per 10,000 live births. Of the total cases, 48.9% were non-Hispanic (NH) white with a crude birth prevalence of 3.4 per 10,000 live births; 12.9% were NH black with a crude birth prevalence of 2.9 per 10,000 live births; 34.8% were Hispanic with a crude birth prevalence of 4.0 per 10,000 live births (Table 1). The overall distribution of race/ethnicity among children with spina bifida in the NBDPN was significantly different from the underlying population ($p<0.001$) (Table 1), with higher proportions of Hispanic children (34.8%) and lower proportions of NH white (48.9%) and NH black children (12.9%) included in the NBDPN, compared with the proportions in the underlying population (28.6%, 51.2% and 15.3%, respectively).

More than half of the children with spina bifida had hydrocephalus (55%), of which 44.4% were diagnosed with Arnold Chiari malformation. The data set provided for this analyses contained only diagnostic information from ICD-9-CM and CDC/BPA diagnostic codes and due to the limited detail of the codes, there is no further information on subtype or lesion level for 69% of the children included in the NBDPN in the present study. Of those that had more detail, most children were diagnosed with the spina bifida subtype Myelomeningocele or related subtype- Meningocele, or Myelocele (92.2%). Of those with a specified level of lesion, most children have a lesion in the lumbar level of the spine (72%); the distribution of other lesion levels include 10.7% sacral, 9.5%

cervical, and 7.8% thoracic. More than half (57%) of the children have at least one additional defect.

As of the last follow-up date in 2010, among all states approximately 7% of the children with spina bifida died before or at the age of 12 months; 75 were fetal deaths and 264 died after birth. Excluding fetal deaths, mean age at death before or at the age of 1 year was 1.9 months. Children without hydrocephalus died at earlier ages (mean age 1.2 months) than those with hydrocephalus (2.5 months) (Table 1). A higher proportion of the NH black children died than NH white and Hispanic children (10.3% vs. 6.2% and 6.7%, respectively). Among the children who died at or before age 1, those of NH white race had a lower mean age of death (1.5 months) compared with NH black and Hispanic children (2.5 months and 2.1 months, respectively).

*Individual states*

The racial and ethnic distributions of the spina bifida cases reflect the underlying population for most states participating in the NBDPN. States tended to have higher proportions of Hispanic children with spina bifida than would be expected based on the underlying state populations (ranging from 0.2 – 9% higher) (Table 5).

*National Spina Bifida Patient Registry*

There are 1,598 eligible children with spina bifida who enrolled from the NSBPR clinic sites for birth years 1999-2007 (Table 2), including 73.6% who were born in the same state as their clinic of enrollment. Among the total enrolled children 52.1% are female. The overall distribution of sex among children in the NSBPR is significantly

different from the distribution in the underlying populations for both the metropolitan ($p=0.009$) and statewide areas ($p=0.009$), with a lower proportion of males compared with the reference population.

Among the total enrolled children 61.8% are NH white race, 7.4% are NH black race, and 23.3% are Hispanic ethnicity. The overall distribution of race/ethnicity among the children in the NSBPR is also significantly different when compared with the distribution among the metropolitan areas ($p<0.001$) and among the statewide areas ($p<0.001$) of the clinic sites. There are a higher proportion of NH white children and a lower proportion of NH black children in the NSBPR compared with both the underlying metropolitan and statewide populations. The proportion of Hispanic children in the NSBPR is similar to that of the underlying statewide population but lower than that of the underlying metropolitan population (Table 2).

More than half of children in the NSBPR have spina bifida with hydrocephalus (63.7%) and most have the spina bifida subtype myelomeningocele (78.6%). The lumbar level of lesion was the most common among these children (59.3%) (Table 2). The mean age of entry into the NSBPR among these children is 6.98 years and five children died after entry into the registry at a mean age of 6.00 years as of the last date of follow-up in 2012.

*Individual Registry Clinic Sites*

The distribution of race/ethnicity among spina bifida cases at clinics participating in NSBPR differs from the corresponding metropolitan and statewide populations (Table 6). Almost all of the sites have a lower proportion of NH black patients than the

proportion of NH black children in both the metropolitan areas (ranging from 2.1 – 18% lower in the NSBPR) and statewide (ranging from 1.4 – 16% lower in the NSBPR). More than half of the sites have a higher proportion of Hispanic patients than the underlying metropolitan populations (ranging from 4.2 – 25.3% higher in the NSBPR), state populations (ranging from 1.8 – 33.3% higher in the NSBPR), or both populations. The relation between the registry sites and the corresponding underlying populations did not follow a consistent pattern across locations for NH white patients.

*States in NBDPN and NSBPR*

There are two states (labeled states X and Y) that participate in both the NBDPN (statewide) and NSBPR (at least one clinic participating). The characteristics of the children with spina bifida in these states were examined after excluding fetal deaths and out-of-state births for the NSBPR sites (Table 3). Assuming that all children born with spina bifida in each state are captured by the NBDPN and that no children move out of the state after birth, the estimated proportion of cases in the NBDPN that are included in the NSBPR is 0.26 for state X and 0.21 for state Y; meaning that approximately one-quarter to one-fifth of children born with spina bifida in state X and Y, respectively, are included in the NSBPR and accessing specialty services at a clinic in that particular state and were invited and chose to enroll in the NSBPR.

For both states, the race/ethnicity distribution of the NBDPN cases is different from that of the NSBPR. The estimated proportion of NBDPN NH black children included in the NSBPR is lower in state X (18%) than in state Y (30%). The estimated proportion of NBDPN Hispanic children included in the NSBPR is higher in state X

(29%) and lower in state Y (15%). The NSBPR in state X has more lipomyelomeningocele subtype cases than were identified in the NBDPN for state X, while State Y has similar proportions of spina bifida subtypes in both systems. The proportion of children who have spina bifida with hydrocephalus is similar across both systems, and across both states.

*Spina bifida subtypes by Race/Ethnicity*

The distribution of spina bifida subtype was similar among NH white and NH black children in the NBDPN and the NSBPR (Table 4). However, Hispanic children were more likely to be diagnosed with the lipomyelomeningocele subtype (12.4%) at birth than NH white (4.8%) and NH black (2.7%). In the NSBPR, the proportion of children with the lipomyelomeningocele subtype was higher than in the NBDPN for all three races and ethnicities, but varied the most for NH white (12.1%) and NH black (11.9%) children. Among the children in the NSBPR, the NH white and NH black children have higher proportions of spina bifida with hydrocephalus cases (64.6% and 68.6%, respectively), when compared with that of Hispanic children (59.8%). Level of lesion was not assessed by race/ethnicity due to limited detail based on diagnostic codes.

**Discussion**

In this study we found that the race/ethnicity distributions of the NBDPN and the NSBPR were significantly different from that of their respective underlying populations, with an under-representation of NH black children. In both the NBDPN and NSBPR, most children had the spina bifida subtype myelomeningocele or related subtype and more than half had hydrocephalus. In both systems, the distribution of spina bifida subtype was similar among NH white and NH black children, but the distribution differed among Hispanic children with these children having a higher proportion of the Lipomyelomeningocele subtype.

The overall crude birth prevalence for spina bifida in the pooled NBDPN (3.2 per 10,000 live births) was similar to previous published birth prevalence estimates (9, 17). The crude birth prevalence estimates stratified by race/ethnicity in the NBDPN were also similar to published birth prevalence estimates (19, 46, 53) and prevalence estimates of children living with spina bifida (20, 85) by race/ethnicity. These findings exhibit the same pattern that spina bifida is less common among NH blacks and more common among Hispanics than NH whites. This same pattern of racial/ethnic distribution was also observed in the NSBPR data.

The race/ethnicity distribution of both the NBDPN and NSBPR were significantly different from the underlying populations. Our analyses support the previously reported observation that the birth prevalence of spina bifida is more common among Hispanics in the United States (19). Hispanic ethnicity has been found to be a risk factor for neural tube defects, and it has been suggested that there may be interactions between ethnic

background and environmental factors among Hispanics (46, 47, 52) including acculturation factors and diet (86, 87).

In the NSBPR, although higher proportions of Hispanic children were enrolled in more than half of the registry clinic sites than in the underlying statewide and metropolitan populations, the overall proportion of Hispanic children in the NSBPR population was similar to that of the underlying statewide population but lower than that of the underlying metropolitan population. Given previous reports of higher prevalence of spina bifida among Hispanics, we would expect the total proportion of Hispanic spina bifida cases in the NSBPR to be higher than the proportion of Hispanics in the underlying population, similar to the pattern seen in the NBDPN. Lower proportions of NH blacks were enrolled overall in the NSBPR compared with the underlying population. While we would expect the proportions of NH blacks with spina bifida to be lower, this group was lower across almost all registry clinic sites including areas with higher concentrations of NH black children in the underlying populations. Racial and ethnic health care inequities have been observed for children with chronic health conditions (77). Our findings may suggest that NH black and Hispanic children might be less likely to access care at one of the clinics. Previous studies have shown that minority children with special health care needs are less likely to have a usual source of care and more likely to use emergency care (88, 89). One study found that Hispanic children with special health care needs experienced more barriers to accessing care and utilized services at lower rates than non-Hispanic children (88). Further studies have suggested that disparities in access to health care experienced by minority children increases the likelihood of experiencing disparities in health outcomes related to existing chronic illnesses or disabilities (89). NH black and

Hispanic children also may be less likely to be offered enrollment into the registry if they attend the clinic than NH white children (90), or they may be less likely to consent to enroll into the registry than NH white children due to attitudes held toward research participation (91, 92). Further exploration of the factors contributing to this race/ethnicity difference among those enrolling from the clinic sites could aid in explaining why this race/ethnicity disparity exists.

As expected, the majority of children in the NBDPN who died did so during the first year, at a mean age of almost 2 months. These findings are consistent with survival studies that have found that mortality of children born with spina bifida occurs most frequently in the first year (18, 73, 93). The finding of a higher proportion of NH black children dying is consistent with previous results where survival among NH blacks and Hispanics with spina bifida has been consistently lower than among NH whites (85, 93). Although further studies are needed to examine the factors that influence race and ethnic disparities in survival, such as access to health care, this consistent pattern could partially explain the lower proportion of NH black children included in the NSBPR. In the NSBPR very few children died after enrollment in the registry, and the mean age of death was much older. The registry was not established until 2009, and the children born in the years 1999-2007 were older when enrolled into the registry so these early deaths would not have been captured among this birth cohort. These children were also not followed for very long; therefore deaths among the children in the registry cannot be extrapolated in this study.

Most children in the NBDPN have the myelomeningocele or related subtype, seen among all race/ethnicity groups; a similar pattern was seen in the NSBPR with more than

80% of children with that subtype, consistent with previous studies and reports (6, 9). Also, consistent with previous findings, in both the NBDPN and the NSBPR the ratio of myelomeningocele or related subtype to lipomyelomeningocele subtype among Hispanics is different from that of NH whites and NH blacks (9). There was a higher proportion of the lipomyelomeningocele subtype in NH white and NH black children in the NSBPR compared with the NBDPN. This could be attributed to functionality and mobility because patterns and frequency of musculoskeletal clinical signs and symptoms in patients with lipomyelomeningocele differ from myelomeningocele patients (94). Children with lipomyelomeningocele might be more mobile and more able to travel to the clinics to seek care. One study found that children with myelomeningocele had poorer walking ability, poorer bladder and bowel function, and significantly lower mobility and social function compared with children with lipomyelomeningocele (80). While we expect to see higher proportions of children with the myelomeningocele or related subtype, the higher than expected proportion of children with lipomyelomeningocele in the NSBPR could be attributed to the increased mobility among these children or higher rates of survival after birth of this spina bifida subtype. The natural history of lipomyelomeningocele remains largely unknown, but the pathogenic mechanism is likely different from myelomeningocele subtypes (6). Further studies of this subtype could help clarify why this pattern is seen and inform care strategies since there are a large proportion of children receiving care with this subtype.

In the NSBPR, the majority of patients have spina bifida located in the lumbar level, consistent with previous reports (6, 9). However, almost one third of patients have a lesion in the sacral level, which is seen consistently across race/ethnicity groups. The

level of the lesion is potentially related to survival and long-term quality of life (63, 82), and the higher the occurrence of the lesion, typically, the more severe the defect (6, 10). Previous studies suggest that cervical lesions are associated with lower survival than lumbar lesions (93, 95). This might explain our findings of more children in the NSBPR with lesions in the lumbar and sacral levels. Information on lesion level was not available for more than half of the children in the NBDPN; most of the individual states had unspecified lesion level information for more than 55% of the children born with spina bifida. Therefore it is difficult to extrapolate the findings.

Many of our findings are consistent with patterns from previously published studies. Population-based surveillance enables the estimation of future service needs based on birth defects prevalence. These estimates allow for predicting demand for accessible resources such as service providers, multidisciplinary clinics, and social and educational services for children born with birth defects (70, 71). While population-based surveillance such as the NBDPN allows for the estimation of service needs quantitatively, the NSBPR can obtain an accurate report of the relationship between treatments and health outcomes based on disease severity (74). Patient registries have the potential to be powerful tools for advancing knowledge in understanding disease progression and management, especially for rare diseases such as spina bifida. In addition, maintaining aggregated national demographic and health outcomes data on children and youth with rare illnesses and special health care needs is critical for identifying and understanding health disparities (77). Both systems have the potential to contribute to the understanding of survival among children with spina bifida. Survival and prevalence estimation using population-based surveillance can be useful in understanding who among children born

with spina bifida are surviving and not surviving, and what characteristics are associated with this survival. The patient registry can be useful in understanding what characteristics are associated with those who are surviving and accessing care at multidisciplinary clinics and the type of care they are receiving. With children continuing to be born with spina bifida and surviving beyond infancy, the objectives of both of these systems are useful and informative in contributing to a better understanding of the condition and improved care and quality of life for children and adults living with spina bifida.

This study had several limitations, the largest being the inability to directly compare the two populations because different children are included from different geographic locations and different information is collected. The NBDPN is population-based, and therefore we are assuming that nearly all children born with spina bifida to residents of these areas are ascertained and included in this surveillance system. However, in the NBDPN the detailed information on spina bifida subtype and lesion level is limited for most states due to the use of general spina bifida diagnostic codes in the available data, resulting in much unknown information. Many states do collect the additional detail on lesion level, but that information was not available in this pooled dataset. Because of this, there is a concern of misspecification due to the need to group the subtypes into similar defect classifications and there may not be homogeneity across subtypes. The NBDPN does not include information on Fatty/Thickened Filum in their case definition of spina bifida because it is considered a spina bifida occulta subtype; therefore population-based information is not available on these cases.

The NSBPR is clinic-based; therefore, we are able to capture detailed and likely accurate information on the clinical characteristics of children with spina bifida such as

subtype and lesion level. However selection bias is a major concern because not everyone with spina bifida is accessing care at multidisciplinary clinics. Multidisciplinary clinic utilization differences may be due to disease severity, referral patterns, or access to health care. Additionally, there may be selection bias in that not all who attend the clinic are invited to participate in the NSBPR, and not all who are invited to participate consent to enroll. There is also potential for volunteer bias because patients in the registry must agree to participate, and those willing to participate might be systematically different from those that don't. An additional limitation is that we are unable to account for residential mobility. The underlying population for the NSBPR may not represent the true source population if people move in and out, especially if this movement differs by race/ethnicity or spina bifida subtype. There may also be selection bias related to race/ethnicity, those children included in the registry may not be representative of the entire race. The NSBPR does not have information on patients with cervical lesions; this could be due to these clinics not seeing patients with these types of lesions for reasons such as survival or mobility. Due to these potential biases, clinical and disease progression information may not be available for certain groups that have spina bifida who are not seeking care at a multidisciplinary clinic. The limitations of both systems highlight the importance and utility of each in continuing to understand the burden, progression, and management of spina bifida in children.

**Conclusions**

This study highlights the utility of both a population-based surveillance system and a clinic-based patient registry in understanding the characteristics of children with spina bifida. Surveillance systems assist in quantitatively evaluating the burden of spina bifida in the population, and patient registries are useful in understanding the clinical characteristics of spina bifida patients. The analyses of these two populations suggest that similar overall patterns are seen in both but that the characteristics of children with spina bifida differ by race/ethnicity and vary geographically. The race/ethnicity characteristics of children included in the NBDPN and NSBPR do not reflect the underlying populations. The NBDPN may not reflect the underlying population because of the burden of disease on the different race/ethnicities, and the NSBPR may not reflect the underlying population because of access to care and utilization of care by the different race/ethnicity groups. With continuing improved survival of children born with spina bifida, the burden on health care, especially for multidisciplinary clinics will increase, and further information collected and drawn from a population-based system and clinic-based system will be useful in improving the care and quality of life of children with spina bifida.

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**Table 1. Demographic and clinical characteristics of children born with spina bifida in the years 1999-2007 among 9 states that are included in the National Birth Defects Prevention Network (n=3,685); and the sex and race distribution of the underlying populations of the surveillance networks.**

| | NBDPN (n= 3,685) | | Total Births [a] | Crude Birth Prevalence [b] |
|---|---|---|---|---|
| | ***N*** | ***%*** | ***%*** | ***per 10,000 live births*** |
| Sex | | | | |
| Male | 1,814 | 49.2 | 51.2 | 3.3 |
| Female | 1,838 | 49.9 | 48.8 | 3.6 |
| Missing/Unknown | 33 | 0.9 | | |
| Race/Ethnicity [c] | | | | |
| Non-Hispanic White | 1,802 | 48.9 | 51.2 | 3.4 |
| Non-Hispanic Black/African American | 474 | 12.9 | 15.3 | 2.9 |
| American Indian/Alaska Native | 33 | 0.9 | 0.8 | 4.1 |
| Asian/Pacific Islander | 49 | 1.3 | 3.2 | 1.4 |
| Hispanic/Latino | 1,281 | 34.8 | 28.6 | 4.0 |
| Other or Multi Race | 16 | 0.4 | 0.8 | 1.7 |
| Unknown/Unspecified | 30 | 0.8 | | |
| Subtype [d] | | | | |
| Myelomeningocele or related | 3,398 | 92.2 | | |
| Lipomyelomeningocele | 287 | 7.8 | | |
| Hydrocephalus | | | | |
| With Hydrocephalus | 2,028 | 55.0 | | |
| Arnold Chiari Malformation | 901 | 44.4 | | |
| Stenosed Aqueduct of Sylvius | 98 | 4.8 | | |
| Without | 1,657 | 45.0 | | |
| Level of Lesion [e] | | | | |
| Cervical | 108 | 2.9 | | |
| Thoracic | 88 | 2.4 | | |
| Lumbar | 816 | 22.1 | | |
| Sacral | 121 | 3.3 | | |
| Unknown/Unspecified | 2,552 | 69.3 | | |
| Case Type [f] | | | | |
| Isolated | 1,509 | 41.0 | | |
| Multiple major defects | 2,176 | 59.1 | | |
| At least one minor defect | 17 | 0.5 | | |
| Vital Status | | | | |
| Live | 3,306 | 89.7 | | |
| Deceased before or at age 12 months | 264 | 7.2 | | |
| Fetal death | 75 | 2.0 | | |
| Unknown/Unspecified | 14 | 0.4 | | |
| | ***N*** | ***mean (months) ± SD*** | | |
| Mean age at death [g] | 249 | 1.9 ± 3.3 | | |
| Mean age at death by Subtype [d] | | | | |
| Myelomeningocele or related | 243 | 1.9 ± 3.3 | | |
| Lipomyelomeningocele | 5 | 1.9 ± 2.8 | | |
| Mean age at death by Hydrocephalus | | | | |
| With Hydrocephalus | 128 | 2.5 ± 3.5 | | |
| Without | 121 | 1.2 ± 2.9 | | |
| Mean age at death by Level of Lesion [e] | | | | |
| Cervical | 6 | 1.0 ± 1.3 | | |
| Thoracic | 11 | 0.8 ± 1.5 | | |
| Lumbar | 61 | 1.3 ± 2.6 | | |
| Sacral | 9 | 1.0 ± 2.7 | | |
| Unknown/Unspecified | 162 | | | |

a Total births denominator data was provided by each surveillance system participating in the NBDPN
b The crude birth prevalence was calculated by dividing the number of spina bifida cases by the number of total births, expressed as per 10,000 live births
c Infant race/ethnicity is classified based on maternal race/ethnicity because information on the infant is not available
d Myelomeningocele or related subtype includes subtypes myelomeningocele, myelocele, meningocele, and myelocystocele. These are grouped together because the etiologies are thought to be similar
e Information on level of lesion was based on ICD-9 or CDC/BPA diagnostic codes
f Isolated case type is defined as those with only a spina bifida diagnosis
g Mean age at death calculations are of deaths that occurred before or at the age of 12 months and exclude fetal deaths

**Table 2. Demographic and clinical characteristics of children with spina bifida born in the years 1999-2007 included in the National Spina Bifida Patient Registry among the 19 clinical sites (n=1,598); and the sex and race distribution of the underlying metropolitan and statewide underlying populations of the participating registry clinics.**

| | NSBPR (n= 1598) | | Total Statewide Births [a] | Total Metropolitan Births [b] |
|---|---|---|---|---|
| | ***N*** | ***%*** | ***%*** | ***%*** |
| Sex | | | | |
| Male | 765 | 47.9 | 51.2 | 51.2 |
| Female | 833 | 52.1 | 48.9 | 48.9 |
| Race/Ethnicity | | | | |
| Non-Hispanic White | 987 | 61.8 | 56.9 | 47.5 |
| Non-Hispanic Black/African American | 118 | 7.4 | 12.1 | 12.5 |
| American Indian/Alaska Native | 4 | 0.3 | 0.6 | 0.4 |
| Asian/Pacific Islander | 93 | 5.8 | 5.5 | 7.8 |
| Hispanic/Latino | 373 | 23.3 | 24.8 | 31.8 |
| Other/Unknown | 23 | 1.4 | | |
| Subtype | | | | |
| Myelomeningocele | 1,256 | 78.6 | | |
| Meningocele | 46 | 2.9 | | |
| Lipomyelomeningocele | 226 | 14.1 | | |
| Other- Fatty/Thickened Filum | 70 | 4.4 | | |
| Hydrocephalus [c] | | | | |
| With Hydrocephalus | 958 | 63.7 | | |
| Without | 547 | 36.4 | | |
| Level of Lesion [d] | | | | |
| Thoracic | 136 | 8.5 | | |
| Lumbar | 947 | 59.3 | | |
| Sacral | 515 | 32.2 | | |
| | ***N*** | ***mean (years) ± SD*** | | |
| Mean Age of Entry into Registry (years) | | 6.9 ± 2.9 | | |
| Vital Status | | | | |
| Live | 1,593 | 99.7 | | |
| Deceased | 5 | 0.3 | | |
| Mean Age of Death (years) | | 6.0 ± 2.8 | | |

a Total statewide births in the years 1999-2007 in the NCHS bridged-race population estimates for the states of the clinic sites in the NSBPR
b Total metropolitan births in the years 1999-2007 in the NCHS bridged-race population estimates for the respective counties of the metropolitan areas of the clinic sites
c Shunt placement in a patient is used as a proxy for presence of hydrocephalus
d Cervical lesion level information is not collected by the NSBPR

**Table 3. Demographic and clinical characteristics among children with spina bifida born years 1999-2007 for 2 states that contain at least one registry clinic included in the NSBPR and a statewide surveillance program included in the NBDPN.**

| | State X | | | State Y | | |
|---|---|---|---|---|---|---|
| | **NBDPN** | **NSBPR In state birth [a]** | **Estimated Proportion of NBDPN Cases in NSBPR [b]** | **NBDPN** | **NSBPR In state birth [a]** | **Estimated Proportion of NBDPN Cases in NSBPR [b]** |
| | ***N (%)*** | ***N (%)*** | | ***N (%)*** | ***N (%)*** | |
| Total Spina Bifida Patients | 420 | 110 | 0.3 | 209 | 43 | 0.2 |
| Sex | | | | | | |
| Male | 200 (47.6) | 44 (40.0) | 0.2 | 90 (43.1) | 19 (44.2) | 0.2 |
| Female | 216 (51.4) | 66 (60.0) | 0.3 | 119 (56.9) | 24 (55.8) | 0.2 |
| Unknown | 4 (0.9) | 0 | | 0 | 0 | |
| Race/Ethnicity [c] | | | | | | |
| NH White | 229 (54.5) | 57 (51.8) | 0.3 | 111 (53.1) | 25 (58.1) | 0.2 |
| NH Black/African American | 68 (16.2) | 12 (10.9) | 0.2 | 33 (15.8) | 10 (23.3) | 0.3 |
| American Indian/Alaska Native | 1 (0.2) | 0 | 0 | 4 (1.9) | 0 | 0 |
| Asian/Pacific Islander | 9 (2.1) | 8 (7.3) | 0.9 | 0 | 0 | 0 |
| Hispanic/Latino | 112 (26.7) | 33 (30.0) | 0.3 | 54 (25.8) | 8 (18.6) | 0.2 |
| Other/Unknown | 1 (0.2) | 0 | 0 | 7 (3.4) | 0 | 0 |
| Vital Status [d] | | | | | | |
| Deceased | 35 (8.3) | 1 (0.9) | | 17 (8.1) | 0 | |
| Subtype [e] | | | | | | |
| Myelomeningocele or related | 407 (96.9) | 65 (59.1) | | 172 (82.3) | 36 (83.7) | |
| Lipomyelomeningocele | 13 (3.1) | 24 (21.8) | | 37 (17.7) | 7 (16.3) | |
| Other- Fatty/Thickened Filum | | 21 (19.1) | | | 0 | |
| Level of Lesion [f] | | | | | | |
| Cervical | 1 (0.2) | | | 0 | | |
| Thoracic | 6 (1.4) | 10 (9.1) | | 6 (2.9) | 4 (9.3) | |
| Lumbar | 64 (15.2) | 45 (40.9) | | 36 (17.2) | 21 (48.8) | |
| Sacral | 6 (1.4) | 55 (50.0) | | 8 (3.8) | 18 (41.9) | |
| Unknown/Unspecified | 343 (81.7) | | | 159 (76.1) | | |
| Hydrocephalus [g] | | | | | | |
| With Hydrocephalus | 196 (46.7) | 47 (42.7) | | 133 (63.6) | 28 (65.1) | |
| Without | 224 (53.3) | 63 (57.3) | | 76 (36.4) | 15 (34.9) | |

a Children who are included in the NSBPR that were born in the state that the registry clinic is located in

b The percent of children that are recorded in the NBDPN that are included in the NSBPR for the particular state. This is calculated by dividing number of children in the NSBPR that are born in the respective state by the number of children included in the NBDPN for that state

c For the NBDPN, infant race/ethnicity is classified based on maternal race/ethnicity because information on the infant is not available

d Vital status for the NBDPN is based upon follow-up through 12 months of age, and excludes fetal deaths

e Myelomeningocele or related subtype includes subtypes myelomeningocele, myelocele, meningocele, and myelocystocele. These are grouped together because the etiologies are thought to be similar, and the NBDPN has limited detail on the specific subtypes

f Information on level of lesion was based on ICD-9 or CDC/BPA diagnostic codes; Cervical lesion level information is not collected by the NSBPR

g For the NSBPR, shunt placement in a patient is used as a proxy for presence of hydrocephalus

**Table 4. Distribution of Spina Bifida Subtypes by Race/Ethnicity among children with spina bifida born years 1999-2007 and included in the National Spina Bifida Patient Registry of children born (n=1,598), and children with spina bifida born years 1999-2007 included in the National Birth Defects Prevention Network (n=3,685).**

| | **Non-Hispanic White** | | **Non-Hispanic Black** | | **Hispanic** | | **Other / Multi-Racial** | | **Unspecified** | | **Total** | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | NBDPN | NSBPR | NBDPN | NSBPR | NBDPN | NSBPR | NBDPN | NSBPR | NBDPN | NSBPR | NBDPN | NSBPR |
| | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* | *N (%)* |
| Sex | | | | | | | | | | | | |
| Male | 881 (48.9) | 465 (47.1) | 241 (50.8) | 69 (58.5) | 635 (49.6) | 175 (46.9) | 46 (46.9) | 45 (46.4) | 11 (45.8) | 11 (47.8) | 1,814 (49.3) | 765 (47.9) |
| Female | 904 (50.2) | 522 (52.9) | 231 (48.7) | 49 (41.5) | 641 (50.0) | 198 (53.1) | 52 (53.1) | 52 (53.6) | 10 (41.7) | 12 (52.2) | 1,838 (50.0) | 833 (52.1) |
| Unknown/Unspecified | 17 (0.9) | 0 | 2 (0.4) | 0 | 5 (0.4) | 0 | 0 | 0 | 3 (12.5) | 0 | 27 (0.7) | 0 |
| Subtype [a] | | | | | | | | | | | | |
| Myelomeningocele or related | 1,716 (95.2) | 829 (84.0) | 461 (97.3) | 104 (88.1) | 1,122 (87.6) | 298 (79.89) | 89 (90.8) | 49 (50.5) | 23 (95.8) | 22 (95.7) | 3,411 (92.7) | 1,302 (81.5) |
| Lipomyelomeningocele | 86 (4.8) | 119 (12.1) | 13 (2.7) | 14 (11.9) | 159 (12.4) | 57 (15.28) | 9 (9.2) | 35 (36.1) | 1 (4.2) | 1 (4.3) | 268 (7.3) | 226 (14.1) |
| Fatty/Thickened Filum | 0 | 39 (3.9) | 0 | 0 | 0 | 18 (4.83) | 0 | 13 (13.4) | 0 | 0 | 0 | 70 (4.4) |
| Hydrocephalus [b] | | | | | | | | | | | | |
| With Hydrocephalus | 955 (53.0) | 638 (64.6) | 265 (55.9) | 81 (68.6) | 744 (58.1) | 223 (59.8) | 48 (49.0) | 18 (18.6) | 12 (50.0) | 17 (73.9) | 2,024 (55.0) | 977 (61.1) |
| Without | 847 (47.0) | 349 (35.4) | 209 (44.1) | 37 (31.4) | 537 (41.9) | 150 (40.2) | 50 (51.0) | 79 (81.4) | 12 (50.0) | 6 (26.1) | 1,655 (45.0) | 621 (38.9) |

a Myelomeningocele or related subtype includes subtypes myelomeningocele, myelocele, meningocele, and myelocystocele. These are grouped together because the etiologies are thought to be similar, and the NBDPN has limited detail on the specific subtypes

b For the NSBPR, shunt placement in a patient is used as a proxy for presence of hydrocephalus

**Table 5. Demographic characteristics of children with spina bifida born in the years 1999-2007 and included in the 9 state population-based surveillance systems of the National Birth Defects Prevention Network, total statewide births information for each participating system's state and the crude spina bifida prevalence for each location.**

| State | | Spina Bifida Cases | Sex | | | Race/Ethnicity [a] | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | Female | Male | Missing | NH White | NH Black | American Indian/Alaska Native | Asian/Pacific Islander | Hispanic | Other/ Multiracial | Unknown |
| **1** | Spina Bifida *N (%)* [b] | 304 | 164 (54.0) | 139 (45.7) | 1 (0.3) | 114 (37.5) | 10 (3.3) | 19 (6.3) | 1 (0.3) | 152 (50.0) | 0 | 8 (2.6) |
| | All Births *%* [c] | | 48.9 | 51.1 | 0 | 43.3 | 3.2 | 6.3 | 2.6 | 42.9 | | |
| | Spina Bifida Prevalence [d] (per 10,000 live births) | | 4.1 | 3.3 | | 3.2 | 3.8 | 3.7 | 0.5 | 4.3 | | |
| **2** | Spina Bifida *N (%)* [b] | 628 | 323 (51.4) | 305 (48.6) | 0 | 321 (51.1) | 130 (20.7) | 3 (0.5) | 6 (1.0) | 165 (26.3) | 1 (0.2) | 2 (0.3) |
| | All Births *%* [c] | | 48.8 | 51.2 | 0 | 48.5 | 21.7 | 0.3 | 2.5 | 26.1 | | |
| | Spina Bifida Prevalence [d] (per 10,000 live births) | | 3.4 | 3.1 | | 3.4 | 3.1 | 5.5 | 1.2 | 3.3 | | |
| **3** | Spina Bifida *N (%)* [b] | 127 | 49 (38.6) | 72 (56.7) | 6 (4.7) | 43 (33.9) | 43 (33.9) | 2 (1.6) | 2 (1.6) | 30 (23.6) | 1 (0.2) | 6 (4.7) |
| | All Births *%* [c] | | 51.0 | 49.0 | 0 | 42.1 | 35.8 | 0.20 | 4.6 | 15.3 | | |
| | Spina Bifida Prevalence [d] (per 10,000 live births) | | 2.1 | 3.2 | | 2.2 | 2.6 | 1.0 | 1.0 | 4.3 | | 1.0 |
| **4** | Spina Bifida *N (%)* [b] | 471 | 241 (51.2) | 224 (47.6) | 6 (1.3) | 260 (55.2) | 76 (16.1) | 1 (0.2) | 11 (2.3) | 121 (25.7) | 0 | 2 (0.4) |
| | All Births *%* [c] | | 48.9 | 51.1 | 0 | 54.7 | 17.6 | 0.1 | 4.8 | 22.8 | | |
| | Spina Bifida Prevalence [d] (per 10,000 live births) | | 3.0 | 2.7 | | 2.9 | 2.6 | 4.7 | 1.4 | 3.2 | | |
| **5** | Spina Bifida *N (%)* [b] | 577 | 289 (50.1) | 286 (49.6) | 2 (0.4) | 434 (75.2) | 88 (15.3) | 3 (0.5) | 15 (2.6) | 36 (6.2) | 0 | 1 (0.2) |
| | All Births *%* [c] | | 48.8 | 51.2 | 0 | 72.4 | 17.5 | 0.5 | 3.1 | 5.9 | | |
| | Spina Bifida Prevalence [d] (per 10,000 live births) | | 5.0 | 4.7 | | 5.1 | 4.3 | 5.0 | 4.1 | 5.2 | | |
| **6** | Spina Bifida *N (%)* [b] | 115 | 52 (45.2) | 63 (54.8) | 0 | 92 (80.0) | 8 (7.0) | 0 | 0 | 15 (13.0) | | 0 |
| | All Births *%* [c] | | 48.8 | 51.2 | 0 | 77.0 | 5.7 | 1.6 | 2.2 | 13.0 | | |
| | Spina Bifida Prevalence [d] (per 10,000 live births) | | 4.6 | 5.3 | | 5.2 | 6.1 | 0 | 0 | 5.0 | | |
| **7** | Spina Bifida *N (%)* [b] | 275 | 142 (51.6) | 133 (48.4) | 0 | 198 (72.0) | 26 (9.5) | 1 (0.4) | 5 (1.8) | 41 (14.9) | 3 (1.1) | 1 (0.4) |
| | All Births *%* [c] | | 48.8 | 51.2 | 0 | 72.7 | 10.3 | 0.4 | 3.6 | 12.2 | | |
| | Spina Bifida Prevalence [d] (per 10,000 live births) | | 2.5 | 2.2 | | 2.3 | 2.1 | 2.3 | 1.2 | 2.9 | | |
| **8** | Spina Bifida *N (%)* [b] | 231 | 125 (54.1) | 105 (45.5) | 1 (0.4) | 128 (55.4) | 35 (15.2) | 4 (1.7) | 0 | 56 (24.2) | 7 (3.0) | 1 (0.4) |
| | All Births *%* [c] | | 48.8 | 51.2 | 0 | 57.2 | 23.0 | 1.3 | 0.3 | 15.5 | | |
| | Spina Bifida Prevalence [d] (per 10,000 live births) | | 4.1 | 3.3 | | 3.6 | 2.5 | 4.8 | 0 | 5.8 | | |
| **9** | Spina Bifida *N (%)* [b] | 1226 | 581 (47.4) | 628 (51.2) | 17 (1.4) | 407 (33.2) | 100 (8.2) | 4 (0.3) | 11 (0.9) | 691 (56.4) | 4 (0.3) | 9 (0.7) |
| | All Births *%* [c] | | 48.9 | 51.1 | 0 | 36.7 | 11.1 | 0.2 | 3.4 | 48.3 | | |
| | Spina Bifida Prevalence [d] (per 10,000 live births) | | 3.5 | 3.6 | | 3.3 | 2.7 | 6.0 | 1.0 | 4.2 | | |

a Infant race/ethnicity is classified based on maternal race/ethnicity because information on the infant is not available
b The number of spina bifida cases for the respective state-based surveillance system
c Total births denominator data provided by each surveillance system participating in the NBDPN
d The spina bifida birth prevalence was calculated by dividing the number of spina bifida cases by the number of total births for each state, expressed as per 10,000 live births

**Table 6. Demographic characteristics of children with spina bifida born in the years 1999-2007 and included in the 19 individual clinic registry sites of the National Spina Bifida Patient Registry, and total metropolitan and statewide births information for each registry clinic location.**

| Clinic Site | | Patients | Sex | | Race/Ethnicity | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Female | Male | NH White | NH Black | American Indian /Alaska Native | Asian/Pacific Islander | Hispanic | Unknown |
| A | Spina Bifida *N (%)* [a] | 161 | 77 (47.8) | 84 (52.2) | 107 (66.5) | 26 (16.2) | 1 (0.6) | 8 (5.0) | 17 (10.6) | 2 (1.2) |
| | Births Metro Area *%* [b] | | 49.3 | 50.7 | 58.5 | 33.8 | 0.2 | 1.3 | 6.3 | 0 |
| | Births Statewide *%* [c] | | 49.1 | 50.9 | 62.5 | 32.3 | 0.4 | 1.0 | 4.8 | 0 |
| B, C | Spina Bifida *N (%)* [a] | 40 | 16 (40.0) | 24 (60.0) | 16 (40.0) | 2 (5.0) | 0 | 1 (2.5) | 21 (52.5) | 0 |
| | Births Metro Area *%* [b] | | 48.8 | 51.2 | 37.0 | 7.1 | 0.4 | 21.7 | 33.9 | 0 |
| | Births Statewide *%* [c] | | 48.9 | 51.1 | 31.7 | 6.4 | 0.5 | 10.7 | 50.7 | 0 |
| D, E | Spina Bifida *N (%)* [a] | 150 | 78 (52.0) | 72 (48.0) | 12 (8.0) | 4 (2.7) | 0 | 6 (4.0) | 126 (84.0) | 2 (1.3) |
| | Births Metro Area *%* [b] | | 48.9 | 51.2 | 25.5 | 6.8 | 0.3 | 8.8 | 58.7 | 0 |
| | Births Statewide *%* [c] | | 48.9 | 51.1 | 31.7 | 6.4 | 0.5 | 10.7 | 50.7 | 0 |
| F | Spina Bifida *N (%)* [a] | 122 | 56 (45.9) | 66 (54.1) | 70 (57.4) | 0 | 0 | 12 (9.8) | 40 (32.8) | 0 |
| | Births Metro Area *%* [b] | | 48.8 | 51.2 | 56.2 | 5.8 | 0.5 | 3.4 | 34.2 | 0 |
| | Births Statewide *%* [c] | | 48.8 | 51.2 | 60.4 | 5.3 | 0.7 | 3.0 | 30.6 | 0 |
| G | Spina Bifida *N (%)* [a] | 33 | 19 (57.6) | 14 (42.4) | 19 (57.6) | 1 (3.0) | 1 (3.0) | 4 (12.1) | 8 (24.2) | 0 |
| | Births Metro Area *%* [b] | | 48.7 | 51.3 | 76.9 | 12.0 | 0.7 | 4.5 | 18.0 | 0 |
| | Births Statewide *%* [c] | | 48.8 | 51.2 | 65.2 | 12.8 | 0.4 | 4.1 | 17.5 | 0 |
| H | Spina Bifida *N (%)* [a] | 136 | 80 (58.8) | 56 (41.2) | 73 (53.7) | 12 (8.8) | 0 | 12 (8.8) | 39 (28.7) | 0 |
| | Births Metro Area *%* [b] | | 49.0 | 51.1 | 44.5 | 19.2 | 0.2 | 5.7 | 30.5 | 0 |
| | Births Statewide *%* [c] | | 48.9 | 51.1 | 54.5 | 18.1 | 0.2 | 4.2 | 23.0 | 0 |
| I | Spina Bifida *N (%)* [a] | 110 | 51 (46.4) | 59 (46.4) | 88 (80.0) | 5 (4.6) | 0 | 5 (4.6) | 8 (7.3) | 4 (3.6) |
| | Births Metro Area *%* [b] | | 48.7 | 51.3 | 71.2 | 17.5 | 0.2 | 2.1 | 9.0 | 0 |
| | Births Statewide *%* [c] | | 48.8 | 51.2 | 78.2 | 12.3 | 0.2 | 1.4 | 7.9 | 0 |
| J | Spina Bifida *N (%)* [a] | 39 | 26 (66.7) | 13 (33.3) | 26 (66.7) | 2 (5.1) | 0 | 1 (2.6) | 9 (23.1) | 1 (2.6) |
| | Births Metro Area *%* [b] | | 49.5 | 50.5 | 63.0 | 8.8 | 0.2 | 2.6 | 25.5 | 0 |
| | Births Statewide *%* [c] | | 49.0 | 51.1 | 72.5 | 8.9 | 0.2 | 5.8 | 12.5 | 0 |
| K | Spina Bifida *N (%)* [a] | 48 | 22 (45.8) | 26 (54.2) | 28 (58.3) | 14 (29.2) | 0 | 1 (2.1) | 1 (2.1) | 4 (8.3) |
| | Births Metro Area *%* [b] | | 48.7 | 51.3 | 64.8 | 24.6 | 0.4 | 4.2 | 6.1 | 0 |
| | Births Statewide *%* [c] | | 48.8 | 51.2 | 71.5 | 18.7 | 0.6 | 2.8 | 6.4 | 0 |
| L | Spina Bifida *N (%)* [a] | 56 | 33 (58.9) | 23 (41.1) | 34 (60.7) | 11 (19.6) | 0 | 1 (1.8) | 10 (17.9) | 0 |
| | Births Metro Area *%* [b] | | 48.8 | 51.2 | 56.1 | 22.4 | 0.3 | 4.5 | 16.7 | 0 |
| | Births Statewide *%* [c] | | 49.0 | 51.1 | 58.5 | 24.9 | 1.3 | 12.2 | 13.1 | 0 |

a The number of spina bifida patients included in the NSBPR from the respective registry clinic site
b Total metropolitan births in the years 1999-2007 in the NCHS bridged-race population estimates for the respective counties of the metropolitan areas of the clinic sites
c Total statewide births in the years 1999-2007 in the NCHS bridged-race population estimates for the states of the clinic sites in the NSBPR

**Table 6 (continued). Demographic characteristics of children with spina bifida born in the years 1999-2007 and included in the 19 individual clinic registry sites of the National Spina Bifida Patient Registry, and total metropolitan and statewide births information for each registry clinic location.**

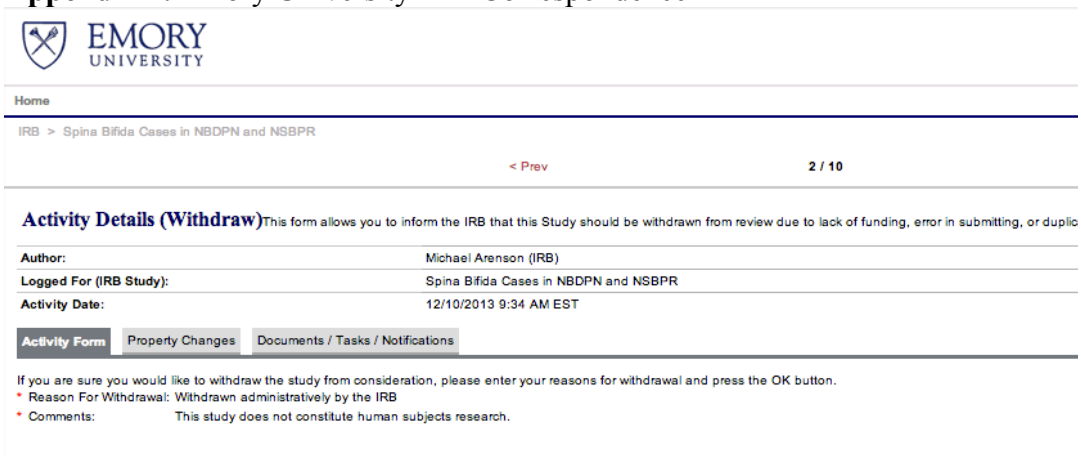
| Clinic Site | | Patients | Sex | | Race/Ethnicity | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | Female | Male | NH White | NH Black | American Indian/ Alaska Native | Asian/ Pacific Islander | Hispanic | Unknown |
| **M** | Spina Bifida *N (%)* [a] | 126 | 70 (55.6) | 56 (44.4) | 99 (78.6) | 7 (5.6) | 0 | 13 (10.3) | 3 (2.4) | 4 (3.20) |
| | Births Metro Area *%* [b] | | 49.1 | 50.9 | 73.9 | 19.5 | 0.2 | 2.5 | 3.8 | 0 |
| | Births Statewide *%* [c] | | 48.9 | 51.1 | 76.7 | 16.5 | 0.2 | 1.8 | 4.8 | 0 |
| **N** | Spina Bifida *N (%)* [a] | 46 | 28 (60.9) | 18 (39.1) | 38 (82.6) | 5 (10.9) | 0 | 1 (2.2) | 2 (4.4) | 0 |
| | Births Metro Area *%* [b] | | 49.0 | 51.0 | 70.0 | 20.4 | 0.3 | 3.5 | 5.8 | 0 |
| | Births Statewide *%* [c] | | 48.9 | 51.1 | 76.7 | 16.5 | 0.2 | 1.8 | 4.8 | 0 |
| **O** | Spina Bifida *N (%)* [a] | 80 | 44 (55.0) | 36 (45.0) | 55 (68.8) | 2 (2.5) | 0 | 3 (3.8) | 19 (23.8) | 1 (1.3) |
| | Births Metro Area *%* [b] | | 48.5 | 51.5 | 65.5 | 4.3 | 1.0 | 6.1 | 23.2 | 0 |
| | Births Statewide *%* [c] | | 48.8 | 51.2 | 78.0 | 16.3 | 0.2 | 1.8 | 3.7 | 0 |
| **P** | Spina Bifida *N (%)* [a] | 62 | 34 (54.8) | 28 (45.2) | 47 (75.8) | 6 (9.7) | 0 | 2 (3.2) | 7 (11.3) | 0 |
| | Births Metro Area *%* [b] | | 48.9 | 51.1 | 76.6 | 12.2 | 0.2 | 2.7 | 8.2 | 0 |
| | Births Statewide *%* [c] | | 49.0 | 51.0 | 73.8 | 14.5 | 0.2 | 3.0 | 8.5 | 0 |
| **Q** | Spina Bifida *N (%)* [a] | 50 | 28 (56.0) | 22 (44.0) | 41 (82.0) | 4 (8.0) | 0 | 1 (2.0) | 4 (8.0) | 0 |
| | Births Metro Area *%* [b] | | 48.9 | 51.1 | 82.3 | 13.6 | 0.2 | 2.2 | 1.8 | 0 |
| | Births Statewide *%* [c] | | 49.0 | 51.0 | 73.8 | 14.5 | 0.2 | 3.0 | 8.5 | 0 |
| **R** | Spina Bifida *N (%)* [a] | 150 | 75 (50.0) | 75 (50.0) | 116 (77.3) | 1 (0.7) | 0 | 6 (4.0) | 22 (14.7) | 5 (3.3) |
| | Births Metro Area *%* [b] | | 48.7 | 51.3 | 72.0 | 2.2 | 0.7 | 4.2 | 20.9 | 0 |
| | Births Statewide *%* [c] | | 48.7 | 51.3 | 80.0 | 1.6 | 1.2 | 2.7 | 14.5 | 0 |
| **S** | Spina Bifida *N (%)* [a] | 104 | 49 (47.1) | 55 (52.9) | 60 (57.7) | 6 (5.8) | 1 (1.0) | 11 (10.6) | 26 (25.0) | 0 |
| | Births Metro Area *%* [b] | | 48.7 | 51.3 | 72.0 | 2.2 | 0.7 | 4.2 | 20.9 | 0 |
| | Births Statewide *%* [c] | | 48.8 | 51.2 | 67.5 | 6.0 | 1.8 | 7.5 | 17.2 | 0 |
| **T** | Spina Bifida *N (%)* [a] | 85 | 47 (55.3) | 38 (44.7) | 58 (68.2) | 10 (11.7) | 1 (1.2) | 5 (5.9) | 11 (12.9) | 0 |
| | Births Metro Area *%* [b] | | 49.3 | 50.7 | 55.4 | 25.1 | 0.6 | 3.9 | 14.9 | 0 |
| | Births Statewide *%* [c] | | 48.9 | 51.1 | 77.6 | 10.0 | 1.2 | 2.9 | 8.3 | 0 |

a The number of spina bifida patients included in the NSBPR from the respective registry clinic site

b Total metropolitan births in the years 1999-2007 in the NCHS bridged-race population estimates for the respective counties of the metropolitan areas of the clinic sites

c Total statewide births in the years 1999-2007 in the NCHS bridged-race population estimates for the states of the clinic sites in the NSBPR

**Appendix 1:** Emory University IRB Correspondence



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**Activity Details (Withdraw)** This form allows you to inform the IRB that this Study should be withdrawn from review due to lack of funding, error in submitting, or duplic

| | |
|---|---|
| **Author:** | Michael Arenson (IRB) |
| **Logged For (IRB Study):** | Spina Bifida Cases in NBDPN and NSBPR |
| **Activity Date:** | 12/10/2013 9:34 AM EST |

Activity Form | Property Changes | Documents / Tasks / Notifications

If you are sure you would like to withdraw the study from consideration, please enter your reasons for withdrawal and press the OK button.

* Reason For Withdrawal: Withdrawn administratively by the IRB
* Comments: This study does not constitute human subjects research.

**Appendix 2.** Centers for Disease Control and Prevention IRB Correspondence

**Subject:** Research Determination 23654: Descriptive analyses of children with spina bifida identified by a clinic-based registry in comparison to those ascertained by state-based population-based surveillance systems

Dear Dr Honein:

The proposed project titled "Descriptive analyses of children with Spina Bifida identified by a clinic-based registry in comparison to those ascertained by state-based population-based surveillance systems " was reviewed by the NCBDDD Human Subjects Contact and determined to be:

**Research NOT involving human subjects**

CDC employees or agents will not obtain identifiable, private information from or about human research participants; based upon the following information provided by the investigator (see attachment and below):

*"Data obtained from the NBDPN and NSBPR will not contain any identifiable, private information about the participants in either system. There will be no engagement with human subjects or collection of data by CDC. CDC does not have access to the data links of the unique identifiers"*

CDC is therefore considered not engaged in human subjects research and this study does not require review by CDC's IRB in accordance with federal regulations (45 CFR 46) for human subjects protections. However, any external research partner's institution(s) who may be engaged in human subjects research must be in compliance with human subjects protections in accordance with federal regulation for the protection of human subjects in research. The NCBDDD Human Subjects contact will work with the PI to make this determination and assist the PI to work with external partners if needed.

If the scope of the project or CDC's role changes beyond that described, you must have the project re-reviewed by the NCBDDD Human Subjects Contact to ensure that CDC is not involved in the conduct of human subjects research and not required to conduct review in accordance with the federal regulations for the protection of human subjects in research.

Please save this email as documentation of the original determination.