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Trends in Survival Among Children With Down Syndrome in 10 Regions of the United States

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Abstract

OBJECTIVE—This study examined changes in survival among children with Down syndrome (DS) by race/ethnicity in 10 regions of the United States. A retrospective cohort study was conducted on 16 506 infants with DS delivered during 1983–2003 and identified by 10 US birth defects monitoring programs. Kaplan-Meier survival probabilities were estimated by select demographic and clinical characteristics. Adjusted hazard ratios (aHR) were estimated for maternal and infant characteristics by using Cox proportional hazard models.

RESULTS—The overall 1-month and 1-, 5-, and 20-year survival probabilities were 98%, 93%, 91%, and 88%, respectively. Over the study period, neonatal survival did not improve appreciably, but survival at all other ages improved modestly. Infants of very low birth weight had 24 times the

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risk of dying in the neonatal period compared with infants of normal birth weight (aHR 23.8; 95% confidence interval [CI] 18.4–30.7). Presence of a heart defect increased the risk of death in the post-neonatal period nearly fivefold (aHR 4.6; 95% CI 3.9–5.4) and continued to be one of the most significant predictors of mortality through to age 20. The postneonatal aHR among non-Hispanic blacks was 1.4 (95% CI 1.2–1.8) compared with non-Hispanic whites and remained elevated by age 10 (2.0; 95% CI 1.0–4.0).

CONCLUSIONS—The survival of children born with DS has improved and racial disparities in infant survival have narrowed. However, compared with non-Hispanic white children, non-Hispanic black children have lower survival beyond infancy. Congenital heart defects are a significant risk factor for mortality through age twenty.

Keywords

Down syndrome; survival; mortality; congenital heart defects; epidemiology; low birth weight; population-based; racial disparities

Down syndrome (DS) is the most common chromosomal disorder among live births and occurs in 1 in every 700 live births in the United States.¹ DS is associated with premature mortality and an increased risk for a number of co-morbid conditions including cardiac, gastrointestinal, musculoskeletal or orthopedic, ear and hearing, ophthalmic, endocrine, leukemia, and autism.² Even though trends in the total birth prevalence of DS have been difficult to determine because of the lack of reliable data on trends in the number of DS-related fetal deaths, the birth prevalence of DS has increased in recent decades in the United States and many other countries.^{3,4} These trends are due in part to an increasing proportion of births to women over age 35.^{3,4}

Although the survival probability for children with DS has improved in recent years,^{5,6} the overall fatality among infants with DS remains more than 5 times higher than that of general population.^{7,8} Furthermore, there is evidence that survival is lower for black children with DS than for white children with DS; however, the reason for the higher fatality rates among blacks is unknown.^{7–10} Factors associated with premature mortality among infants and children with DS include the presence of congenital heart defects (CHD), other structural malformations,^{6,9,10} leukemia,⁷ and low birth weight.^{9,11} Whether variations in the prevalence of these risk factors among race/ethnicity groups explain the observed differences in survival is unclear.

In this study, we examined the long-term trends in survival for children with DS and the variation in survival probabilities by maternal and infant characteristics based on data from 10 population-based surveillance programs in the United States. Adjusted hazard ratios (aHRs) were estimated to assess the association between possible prognostic factors and mortality.

METHODS

Data Sources and Case Criteria

Infants born with DS were identified by 10 population-based birth defects monitoring programs located in Arkansas, Georgia (5 central counties of metropolitan Atlanta^{*}), California (11 counties[†]), Colorado, Iowa, New York (New York City excluded), North Carolina, Oklahoma, Texas, and Utah. The birth cohorts available for each program were Arkansas, 1993–2002; Georgia, 1983–2003; California, 1983–2002; Colorado, 1989–2003; Iowa, 1983–2003; New York, 1983–2003; North Carolina, 1989–1993, 1995–2003; Oklahoma, 1994–2003; Texas, 1996–2003; and Utah, 1995–2003. Vital status was ascertained for all births with DS through December 31, 2004, for all of the regions except for Arkansas and California, the follow-up periods of which ended on December 31, 2003, and December 31, 2002, respectively. Infants with karyotype diagnosis of trisomy 21 were classified as DS by using a modified British Paediatrics Association (BPA) coding system in most regions except for New York, where infants with DS were classified by both BPA and *International Classification of Diseases, Ninth Revision, Clinical Modification* (ICD-9-CM) codes, and in the regions of North Carolina and Colorado, where they were classified by ICD-9-CM codes only. Deaths among children with DS were ascertained by linkage with medical records, state vital records, and the National Death Index.³

Children with DS and no death records were considered alive at the end of the study follow-up period and treated as censored observations in the survival analysis. Demographic and clinical characteristics of infants with DS from birth were also collected by the surveillance programs. Infants of <500 g, <20 weeks of gestational age, or with unconfirmed diagnosis of DS were excluded from our study.

Both demographic and clinical characteristics were included as potential risk factors for survival of infants with DS including maternal race/ethnicity (non-Hispanic white, non-Hispanic black, Hispanic, and other), maternal age (<35 years vs ≥35 years), maternal education (<12 years, ≥12 years), sex, birth weight (<1500 g, 1500–2499 g, ≥2500 g), and region. Infants with DS were classified as having a major CHD if their records indicated the presence of ICD-9-CM or BPA codes for CHD (745.000–747.430 and 747.640). Codes for normal physiologic findings in newborns or premature infants (eg, patent foramen ovale, patent ductus arteriosus), minor conditions such as tricuspid insufficiency, or unconfirmed cardiac defects were not considered structural heart defects.

Data Analysis

The survival probabilities at 1 month, 1 year, 5 years, 10 years, and 20 years were estimated by the Kaplan-Meier product-limit method.¹² Greenwood's method was used to calculate the variance of the estimated survival probability and their 95% confidence intervals (CIs).¹³ For those study regions with at least 20 years of follow-up (GA, CA, IA, and NY), the infant survival probabilities and 95% CIs were estimated for 4 birth cohorts (1983–1987, 1988–

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[†] San Francisco and Santa Clara (1983–2003); Stanislaus (1984–2003); Merced (1985–2003); Fresno, Tulare, and San Joaquin (1986–2003); Kern, Kings, and Madera (1987–2003); Los Angeles (1990–2003, excluding 1998).

1992, 1993–1997, 1998–2003), and a trend analysis for the increasing survival over birth cohorts across race/ethnicity was conducted.

A log-rank test was used to determine whether the survival probabilities were significantly different among various levels of potential demographic and clinical risk factors.¹⁴ Cox proportional hazard models were used to estimate unadjusted and adjusted hazard ratios (aHR) for possible prognostic factors.¹⁴ The assumption of proportionality for the hazards was checked by plotting estimated log-cumulative hazard versus log of survival time for different categories of the risk factors. Possible time-dependent trends were also tested to confirm the assumption of proportionality. Final multivariate proportional hazard models were obtained, and the aHRs were estimated for the significant covariates. For the multivariate proportional hazard models, aHRs were estimated assuming survival through the preceding age period. Computations were performed by using SAS-PC (version 9.13; SAS Institute Inc, Cary, NC), and figures were generated by using S-PLUS (version 6.0; Insightful Corp, Seattle, WA). This study was approved by the Institutional Review Board of the Centers for Disease Control and Prevention.

RESULTS

From 1983 to 2003, 16 506 liveborn infants with DS were identified in the 10 regions included in our study. The number of infants ascertained in the regions ranged from 362 in Arkansas to 4686 in California with a median number of 982 infants, and the period of follow-up ranged from 9 years in Texas to 22 years in Georgia, Iowa, and New York (Table 1). Among those with comparable follow-up time (11 years), the regional variation was greatest between Arkansas (87.2%) and Utah (90.7%; $P = .01$).

The overall 1-month and 1-, 5-, and 20-year survival probabilities were 98%, 93%, 91%, and 88%, respectively (Tables 2 and 3), with the highest mortality occurring in the postneonatal period. Over the 20-year study period, neonatal survival did not improve appreciably, but modestly improved survival at older ages was observed for those infants with DS born after 1996 (Table 4).

Univariate analysis demonstrated that survival varied by a number of demographic and maternal characteristics (Table 2 and 3). The greatest variation in survival to 1 year of age was by birth weight. Infants with normal birth weight had a 95% survival to 1 year compared with 56% and 90% survival to infants of very low and low birth weight, respectively. Infants born with a CHD had lower infant survival than those without (90% vs 96%). Infants born to non-Hispanic black and non-Hispanic white mothers had nearly identical neonatal survival, but thereafter infants to non-Hispanic black mothers experienced increasingly lower survival through age 20 (Fig 1). When stratified by birth weight, infants of non-Hispanic black mothers had lower overall survival only among normal and low birth weight (1500–2499 g) infants; among very low birth weight infants (<1500 g), infants of non-Hispanic black mothers had higher survival than infants of either non-Hispanic white or Hispanic mothers.

Restricting the cohort period to the years during which all regions contributed case data (1997–2003), the pooled survival probability to 1 year was 94% (Fig 2). The 1-year survival probability ranged from 92% in Arkansas to 96% in Utah ($P = .02$). For the regions with 20 years of follow-up (GA, CA, IA, and NY), an increasing trend of survival across 4 birth cohort periods was detected ($P = .002$) overall and for each region except for the region of Georgia (data not shown). Trends of improving survival were apparent across the 4 time periods for each major racial/ethnic groups: non-Hispanic white ($P = .0002$), non-Hispanic black (0.0117), and Hispanic (0.0002); however, the greatest improvement in 1-year survival trends was among infants with a major CHD or of birth weight <2500 g (Fig 3).

For those infants with no missing values for the covariates included in the Cox proportional hazard models ($n = 16\,418$), factors associated with an increased risk of death for children with DS were race/ethnicity, maternal age, birth weight, multiple births, and presence of CHD (Table 4). The only factor associated with an increased risk of neonatal death was birth weight. Infants of very low birth weight had 24 times the risk of dying compared with infants of normal birth weight (aHR 23.8; 95% CI 18.4–30.7), and infants of low birth weight had nearly 2.5-fold increased risk (aHR 2.4; 95% CI 1.8–3.2). Among those who survived the neonatal period, birth weight continued to be associated with an increased risk for death by age 1 for very low (aHR 1.9; 95% CI 1.7–2.3) and low (aHR 6.9; 95% CI 5.6–8.6) birth weight infants. The presence of a heart defect increased the risk of death in the postneonatal period nearly fivefold (aHR 4.6; 95% CI 3.9–5.4) and continued to be one of the most significant predictors of mortality through age 20. The aHR among non-Hispanic blacks at age 1 was 1.4 (95% CI 1.2–1.8) compared with non-Hispanic whites and increased to 2.0 (95% CI 1.0–4.0) by age 10. Infants born to Hispanic mothers had a lower aHR at 1 month of age (aHR 0.8; 95% CI 0.6–1.0) and had an overall reduced risk for mortality (aHR 0.8; 95% CI 0.7–0.9) compared with infants born to non-Hispanic white mothers.

DISCUSSION

Survival among individuals with DS has improved in the United States over time, and survival to 1 year now averages 94% among the 10 regions included in this study. With the exception of the neonatal period, survival in the United States improved over time for all age points, and the most significant gains were among infants born of low birth weight or with a major CHD. Although slight racial and ethnic disparities in survival persist, these have decreased markedly over time. Survival estimates to 1 year varied from 92% to 96% among the 10 regions included in the study. Reasons for state variation are unclear but might be the result of different population characteristics, variations in case ascertainment, state-level policies governing eligibility criteria for health care coverage, or variations in the amount and type of public services available.

This is the largest population-based survival study for people with DS using birth defects surveillance programs, which provide a unique source of quality data ascertained from multiple sources for high sensitivity and diagnostic accuracy in the United States. Previous survival estimates in the United States have been limited to individual surveillance programs.^{9,15,16} Data for most of those studies were subsumed by this study to produce the

most nationally representative survival estimates available to date that can serve as a benchmark as well as a comparison point for reports from other countries.

Linkage of surveillance data with the National Death Index ensured the most accurate determination of the vital status of children even if they died out of state and adds significantly to the credibility of the findings¹⁷; however, the assumption that a child was alive if there was no record of death found from the three data sources could be a potential limitation of the study. Additionally, no information on surgeries, clinical management, or barriers to health care as potential contributors to the long-term survival of children with DS was examined.

Factors most associated with an increased risk of mortality among individuals with DS were race/ethnicity, low birth weight, and the presence of CHD. Although some studies have suggested a survival advantage among male children,^{6,18} our study confirmed findings from other studies that found no survival differences by sex^{9,10,19–21} Although previous reports have found an increased risk associated with low birth weight,^{6,9,21} only 1 other population-based study was found that examined very low birth weight infants (<1500 g) as a distinct group, possibly because of relatively low study population sizes.²² This study found that among infants with very low birth weight those with DS had 2.5 times the risk of death compared with very low birth weight infants with no birth defects. The percent of infants with DS in our study population that were born with birth weight <2500 g was 22%, a >2.5-fold increased risk compared with the general population, and these infants were twice as likely to be born <1500 g.²³ Recognition of the high risk of mortality associated with very low birth weight for infants with DS is important to increase vigilance among health care providers for this vulnerable group.

Two previous reports in the United States were inconsistent with regard to racial and ethnic disparities in survival^{9,15}; however, the discrepancy is likely the result of 2 study attributes. First, each used non overlapping time periods of observation, so that the later study (Vendola et al) might reflect the narrowing survival gap as evidenced by the decreasing trend in disparities seen in this study. The second and more compelling reason for the differences in the study findings was that Rasmussen et al presented overall hazard ratios up to 20 years of age, whereas Vendola et al restricted their analysis to the first year of life. Our study showed that association between race and mortality increased with increasing age.

Several studies observed that the greatest black-white disparity occurred among infants with no major CHD, suggesting that more undiagnosed CHD among non-Hispanic blacks might be contributing to the disparity.^{8,9,24,25} Non-Hispanic black infants without a CHD had lower 1-year survival than non-Hispanic whites from 1983 to 1989 (91.3% vs 95.8%), but the disparity nearly disappeared by the 1997–2003 period (97.4% vs 97.7%). To evaluate the potential role of undiagnosed CHD in the black-white disparity, we examined the percent of infants with DS and a CHD by race and over time. During both the earliest and most recent time periods, a greater percent of non-Hispanic blacks with DS was diagnosed with a heart defect compared with non-Hispanic whites: 44% among non-Hispanic blacks versus 41% among non-Hispanic whites during 1983–1989 and 53% among non-Hispanic blacks versus 50% among non-Hispanic whites during 1997–2003. Furthermore, although less severe

CHD such as muscular ventricular septal defects are reported less frequently among non-Hispanic blacks compared with non-Hispanic whites,²⁶ there appear to be little racial/ethnic difference in the birth prevalence of more severe heart defects that would have a greater influence on survival, such as atrioventricular septal defect, the most common heart defect among infants with DS.^{26,27}

Unique to this study was the examination of the changing impact across the life span of factors that contribute to mortality. Goldman et al found age variations in the contribution by specific factors to mortality, but the study was limited to the first year of life.²² Our analysis showed that very low and low birth weight conferred the greatest risk of mortality during the neonatal period, but the associated risk lessened with increasing age. CHDs are the leading cause of death among infants with DS⁸ and conferred a risk of mortality that was highest during the post-neonatal period and was associated with the greatest risk relative to the other factors from age 1 through 10. The mortality risk associated with non-Hispanic black race increased with increasing age even after adjusting for the presence of a heart defect and low birth weight, possibly reflecting inadequate access or utilization of health care services.

The population-based approach of this study is a substantial strength in that it ensures the most complete live-born population of infants with DS. The limitation of this and most survival studies is the lack of accounting for the prenatal experience. Attitudes toward prenatal testing and the use of it vary by a number of maternal factors, including sociodemographic factors, race, and ethnicity.²⁸ The proportion of elective terminations of a fetus with DS in the United States ranged from 7% to 37% with variations by time period and regional racial/ethnic composition.^{29–32} A recent review of population-based studies of pregnancies with a positive prenatal diagnosis of DS estimated that 67% of pregnancies were terminated, but a temporal analysis found that the proportion of electively terminated pregnancies has consistently decreased in recent years.³³ Although information on frequency of termination is scarce and difficult to interpret,^{34,35} evidence suggests that elective terminations might have a significant impact on the epidemiology of live born infants with DS.^{36,37} If the presence of severe comorbid conditions such as major CHD factor into the decision to terminate, the observed decreasing trends in the decision to terminate a pregnancy with a positive diagnosis of DS could be the result of more fetuses with less complicated health profiles being carried to term. This potential scenario would lead to a live birth population with an overall higher likelihood of survival, but the extent to which this might contribute to the recent improvements in survival among children with DS is not clear.

Survival in the United States compares favorably for both short- and long-term survival of individuals with DS. The 93% infant survival in the United States was higher than that reported in the United Kingdom (88%),³⁸ Australia (92%),⁶ Ireland (88%),²⁰ Italy (80%),²¹ and Denmark (85%).³⁹ The 10-year survival of 91% in the United States was also higher than estimates elsewhere, which ranged from 82% to 85%,^{6,20,37} and the 20-year survival rate of 88% was higher than reported elsewhere.³⁷ International comparisons should be made with some caution because differences in ascertainment methods, the time period of observation, and disposition for elective terminations could account for some of the observed differences in infant survival.^{4,40} However, comparison of the longer-term survival

estimates that are likely to be less affected by such factors can become particularly important in planning for health services to address specialized health and social services needs of children, adolescents, and adults with DS. In particular, about half of children with DS have major comorbid conditions such as CHD for which access to timely and quality health care services is critically important not only for survival but also to ensure a reasonable quality of life.

CONCLUSIONS

Survival of individuals with DS has improved over the past 20 years, and the racial and ethnic disparities have diminished, particularly during infancy, potentially as the result of improved access to health care services; however, non-Hispanic blacks still appear to be at greater risk of mortality throughout childhood and adolescence. Improved surgical and medical management of CHD and issues related to low birth weight have contributed to the overall improved survival of those with DS, yet significant risks are still associated with these factors. Population-based survival analyses to date have been limited to the evaluation of demographic and clinical factors present at birth. Linkage of population-based birth defects surveillance data with additional data sources such as hospital discharge data would provide a powerful tool to examine the impact of health care access, quality, and utilization on health outcomes of individuals with DS.

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ABBREVIATIONS

aHR	adjusted hazard ratios
BPA	British Paediatrics Association
CHD	congenital heart defect
CI	confidence interval
DS	Down syndrome

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WHAT'S KNOWN ON THIS SUBJECT

Although survival of children born with Down syndrome has improved, unexplained racial and ethnic disparities in survival persist in the United States.

WHAT THIS STUDY ADDS

This study used population-based data from 10 birth defects monitoring programs in the United States to examine survival trends among children born with Down syndrome and to evaluate the changing influence of survival predictors over the life course.

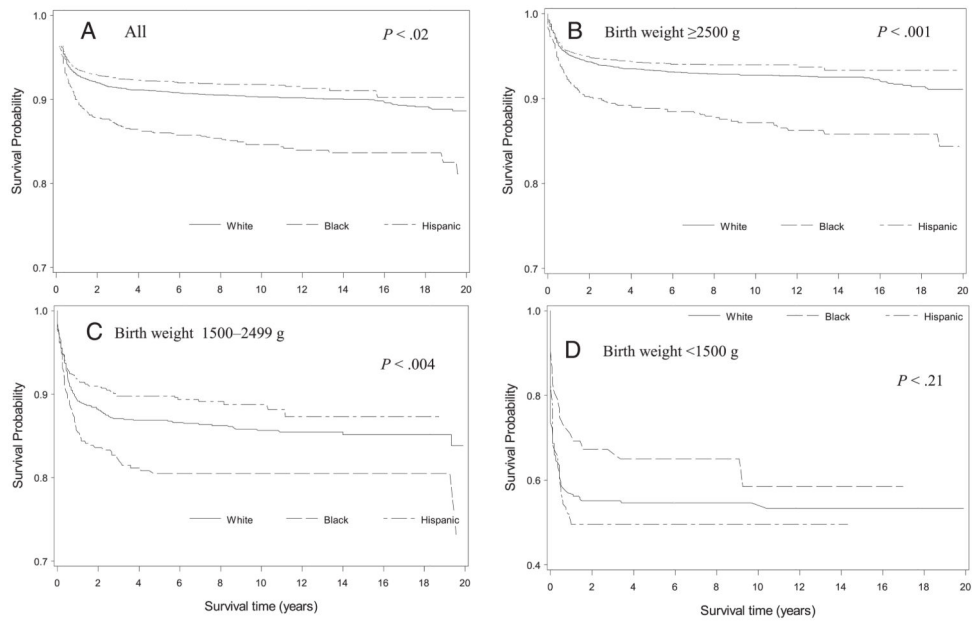


FIGURE 1. Kaplan-Meier survival curves by race and ethnicity and birth weight for individuals born with DS in from 10 US regions, 1983–2003.

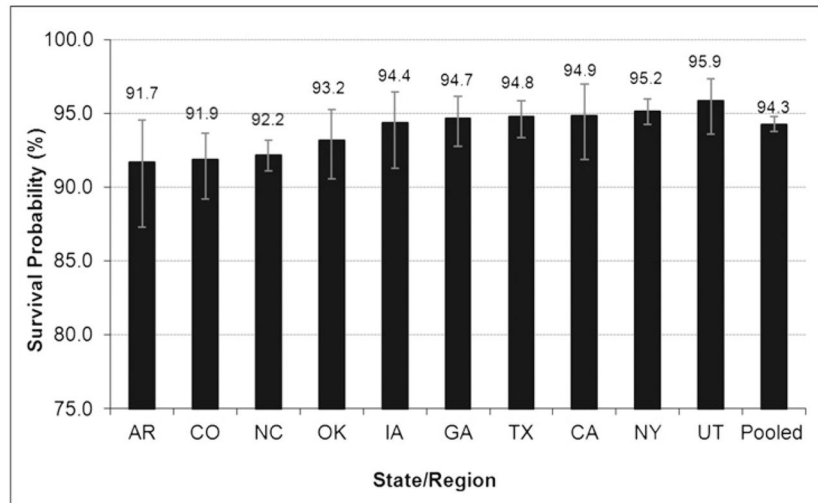


FIGURE 2.
Survival probability to 1 year among children with DS, 1997–2003.

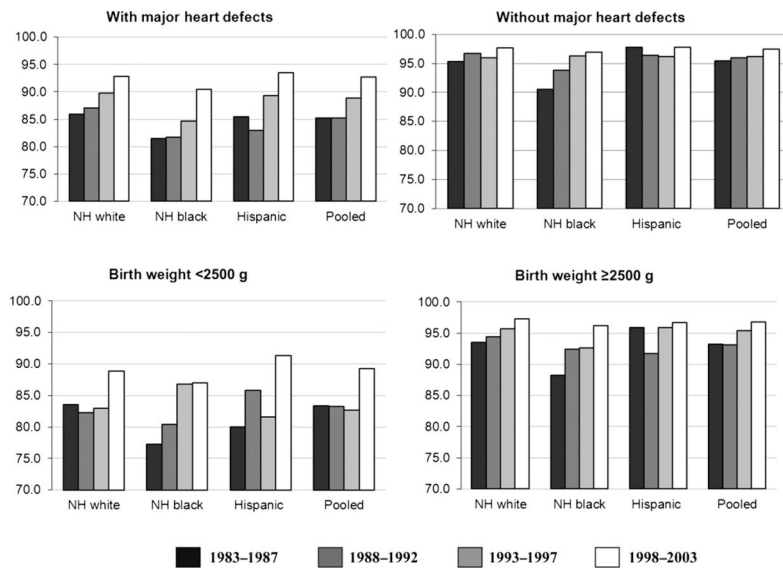


FIGURE 3. Racial/ethnic variation in one year survival of children with Down syndrome in four states/regions (CA, GA, IA, NY) by select clinical characteristics, 1983–2003.

TABLE 1

Sample Size and Years of Observation by Region in Ascending Order of Years of Follow-up

Region	Sample Size	Birth Years	Follow-up Years	Years of Follow-up
Texas	2663	1996–2003	1996–2004	9
Utah	556	1995–2003	1995–2004	10
Arkansas	362	1993–2002	1993–2003	11
Oklahoma	546	1994–2003	1994–2004	11
Colorado	972	1989–2003	1989–2004	16
North Carolina	1628	1989–1993, 1995–2003	1989–2004	16
California	4686	1983–2002	1983–2003	20
Iowa	849	1983–2003	1983–2004	22
New York	3355	1983–2003	1983–2004	22
Georgia	889	1983–2003	1983–2004	22

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Survival Probabilities for Infants With DS by Selected Maternal and Child Characteristics in 10 US Regions During 1983–2003

TABLE 2

	<28 d		1 y		5 y		10 y		20 y	
	Deaths	Survival % (95% CI)	Deaths	Survival % (95% CI)	Deaths	Survival % (95% CI)	Deaths	Survival % (95% CI)	Deaths	Survival % (95% CI)
Total	318	98.1 (97.9–98.3)	1180	92.9 (92.5–93.2)	1489	91.0 (90.5–91.4)	1551	90.7 (90.2–91.1)	1584	88.1 (87.0–89.0)
Mother's race/ethnicity										
Non-Hispanic White	8877	97.9 (97.6–98.2) ^a	618	93.3 (92.5–93.6) ^a	784	90.9 (90.2–91.5) ^a	818	90.3 (89.6–90.9) ^a	839	88.6 (87.5–89.6) ^a
Non-Hispanic Black	1576	97.8 (97.0–98.4) ^a	156	90.2 (88.6–91.6) ^a	209	86.1 (84.2–87.8) ^a	220	84.8 (82.8–86.6) ^a	224	81.5 (75.7–86.1) ^a
Hispanic	5113	98.6 (98.2–98.9) ^a	318	93.8 (93.1–94.4) ^a	383	92.2 (91.4–92.9) ^a	391	91.8 (91.0–92.6) ^a	396	90.2 (88.1–92.0) ^a
Other	863	97.2 (95.8–98.1) ^a	78	91.1 (89.0–92.8) ^a	97	88.4 (86.0–90.4) ^a	104	86.7 (84.0–89.0) ^a	106	85.5 (82.3–88.2) ^a
Missing	77	—	10	—	16	—	18	—	19	—
Infant sex										
Male	8928	97.9 (97.6–98.2)	644	92.8 (92.2–93.3)	800	90.8 (90.1–91.3)	833	90.0 (89.4–90.7)	853	88.2 (87.0–89.4)
Female	7577	98.3 (97.9–98.5)	536	92.9 (92.3–93.5)	689	90.6 (89.9–91.3)	718	89.0 (89.0–90.5)	731	87.9 (86.3–89.2)
Missing	1	—	0	—	0	—	0	—	0	—
Birth wt (g)										
2500	12826	99.0 (98.8–99.2) ^a	637	95.1 (94.7–95.4) ^a	856	93.1 (92.6–93.5) ^a	903	92.3 (91.8–92.8) ^a	927	90.7 (89.9–91.6) ^a
1500–2499	3190	97.7 (97.1–98.2) ^a	327	89.8 (88.7–90.8) ^a	406	86.9 (85.7–88.1) ^a	420	85.9 (84.6–87.2) ^a	426	82.7 (78.3–86.2) ^a
<1500	479	76.6 (72.6–80.2) ^a	211	56.0 (51.4, 60.3) ^a	222	53.3 (48.7–57.7) ^a	223	52.6 (47.8–57.1) ^a	226	48.0 (40.7–55.0) ^a
Missing	11	—	5	—	5	—	5	—	5	—
Maternal age (y)										
<35	10572	98.2 (97.9–98.5)	789	92.6 (92.0–93.0) ^b	1005	90.2 (89.6–90.8) ^c	1046	84.5 (88.9–90.1) ^b	1071	87.5 (86.3–88.6) ^b
35	5933	97.8 (97.4–98.2)	391	93.4 (92.8–94.0) ^b	484	91.6 (90.8–92.2) ^c	505	90.7 (89.9–91.5) ^b	513	89.4 (87.8–90.7) ^b
Missing	1	—	0	—	0	—	0	—	1	—

—, no estimates were produced because of small numbers.

^a $P < .0001$.

^b $P < .05$.

^c $P < .01$.

Survival Probabilities for Infants With DS by Selected Maternal and Child Characteristics in 10 US Regions During 1983–2003

TABLE 3

	<28 d		1 y		5 y		10 y		20 y	
	Deaths	Survival, % (95% CI)	Deaths	Survival, % (95% CI)	Deaths	Survival, % (95% CI)	Deaths	Survival, % (95% CI)	Deaths	Survival, % (95% CI)
Births										
Maternal education (y)										
12	11437	220 98.1 (97.8–98.3)	787 93.1 (92.7–93.6)	995 91.1 (90.5–91.6)	1035 90.3 (89.7–90.9)	404 88.9 (87.9–89.8)				
<12	4132	66 98.4 (98.0–98.7)	309 92.6 (91.7–93.3)	381 90.4 (89.4–91.9)	399 89.3 (88.3–90.3)	1056 86.0 (81.3–89.6)				
Missing	937	32 —	84 —	113 —	117 —	124 —				
Plurality										
Singleton	16048	308 98.1 (97.9–98.3)	1129 93.0 (92.6–93.4) ^a	1425 90.8 (90.4–91.3) ^a	1486 90.1 (89.6–90.5) ^a	1518 88.2 (87.2–89.1) ^a				
Multiple	440	10 97.7 (95.8–98.8)	50 88.6 (85.3–91.2) ^a	61 86.0 (82.3–88.9) ^a	62 85.5 (81.8–88.6) ^a	63 84.4 (79.9–88.0) ^a				
Missing	18	0 —	1 —	3 —	3 —	3 —				
CHDs										
No	8576	176 97.9 (97.6–98.2)	343 96.0 (95.5–96.4) ^b	417 95.0 (94.5–95.5) ^b	444 94.4 (93.8–94.9) ^b	460 93.0 (92.0–93.9) ^b				
Yes	7930	142 98.2 (97.9–98.5)	837 89.6 (88.9–90.2) ^b	1072 86.0 (85.2–86.7) ^b	1107 85.0 (84.1–85.8) ^b	1124 82.2 (80.1–84.1) ^b				
Missing				0 —						
Birth cohort										
1983–1989	2454	51 97.9 (97.2–98.4)	213 91.3 (90.0–92.4) ^b	292 88.1 (86.8–89.3) ^b	310 87.4 (86.0–88.6) ^b	334 85.7 (84.1–87.1) ^b				
1990–1996	5441	109 98.0 (97.6–98.3)	477 91.2 (90.5–92.0) ^b	589 89.2 (88.3–90.0) ^b	624 88.4 (87.6–89.3) ^b	—				
1997–2003	8611	158 98.2 (97.9–98.4)	490 94.3 (93.8–94.8) ^b	608 92.5 (91.9–93.0) ^b	—	—				

—, no estimates were produced because of small numbers.

^a $P < .0001$.

^b $P < .0001$.

aHRs^a for Select Covariates Among Children With Down Syndrome (*n* = 16 418) by Age at Follow-up From 10 US Regions, 1983–2003

TABLE 4

	1 mo	2–12 mo	1–5 y	6–10 y	11–20 y	Overall
Race/ethnicity						
White	Referent	Referent	Referent	Referent	Referent	Referent
Blacks	1.0 (0.7–1.5)	1.4 (1.2–1.8) ^b	1.9 (1.4–2.6) ^b	2.0 (1.0–4.0) ^b	1.7 (0.6–5.1)	1.4 (1.0–1.6)
Hispanics	0.8 (0.6–1.0) ^b	1.0 (0.9–1.2)	0.8 (0.6–1.0)	0.6 (0.3–1.2)	1.7 (0.6–4.7)	0.8 (0.7–0.9) ^b
Other	1.3 (0.8–2.0)	1.3 (1.0–1.7)	1.2 (0.8–2.0)	2.4 (1.1–5.4) ^b	1.9 (0.4–8.0)	1.3 (1.1–1.6) ^b
Birth wt						
2500	Referent	Referent	Referent	Referent	Referent	Referent
1500–2499	2.4 (1.8–3.2) ^b	1.9 (1.7–2.3) ^b	1.4 (1.1–1.9) ^b	1.2 (0.7–2.4)	1.3 (0.5–3.1)	1.8 (1.6–2.0) ^b
<1500	23.8 (18.4–30.7) ^b	6.9 (5.6–8.6) ^b	2.1 (1.2–3.9) ^b	1.1 (0.2–8.2)	8.5 (2.5–28.6) ^b	8.5 (7.3–9.8) ^b
Maternal age						
<35	Referent	Referent	Referent	Referent	Referent	Referent
35 y	1.0 (1.0–1.0)	1.0 (1.0–1.0)	1.0 (1.0–1.0)	1.0 (1.0–1.0)	1.0 (0.9–1.0)	1.0 (1.0–1.0)
CHD, yes vs no (referent)	0.8 (0.6–1.2)	4.6 (3.9–5.4) ^b	4.0 (3.1–5.2) ^b	1.9 (1.1–3.2) ^b	2.0 (1.0–4.0) ^b	2.7 (2.4–3.0) ^b
Birth cohort						
1983–1989	Referent	Referent	Referent	Referent	Referent	Referent
1990–1996	0.9 (0.6–1.2)	1.0 (0.8–1.2)	0.6 (0.5–0.8) ^b	—	—	—
1997–2003	0.8 (0.5–1.1)	0.5 (0.4–0.6) ^b	0.5 (0.4–0.7) ^b	—	—	—

Birth wt reference group is >2500. Survival probability among non-Hispanic blacks, Hispanic, and other was compared with the survival probability among non-Hispanic whites. —, no estimates were produced because of small numbers.

^a Adjusted for race/ethnicity, birth wt, maternal age and education, presence of a CHD, birth period, and region of birth.

^b Statistical difference in survival probabilities between category stratum and the referent group.