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The prevalence of Down syndrome was studied among all live births occurring between 1989 and 1991 in the California counties monitored by the California Birth Defects Monitoring Program. Objectives of this study were: 1) to calculate adjusted prevalence rates and quinquennial maternal age-specific risk rates of Down syndrome after adjusting for elective abortion of prenatally diagnosed fetuses; 2) to estimate the impact of prenatal diagnosis and subsequent elective abortion of affected fetuses on the observed prevalence of Down syndrome; and 3) to examine sex ratios among liveborn infants and fetuses with Down syndrome. The racial/ethnic diversity and large size of the population allowed the data to be stratified into five racial categories—Hispanics, whites, Asians, blacks, and others. For the period 1989–1991, the observed prevalence of Down syndrome was 1.13 per 1,000 live births, and the adjusted total prevalence, which took into account the termination of affected pregnancies following prenatal diagnosis, was 1.53 per 1,000 live births. In a comparison of quinquennial maternal age-specific risk rates of Down syndrome by race, Hispanics and whites were the only groups with rates that differed significantly from each other, with Hispanics exhibiting higher rates at maternal ages under 40 years. The overall reduction in live births with Down syndrome in 1989–1991 that could be attributed to prenatal diagnosis and elective abortion of affected fetuses was 25.8%, with a 49.1% reduction being observed at maternal ages ≥ 35 years. In 1990–1991, Hispanics had the lowest overall reduction (10.0%), while whites had the highest reduction (46.3%). The male:female ratios among liveborns with Down syndrome were significantly higher than those among all live births, and race had a significant association with sex ratios in both cases and controls. These findings indicate that prenatal diagnosis and elective termination of affected pregnancies has had a substantial impact in reducing the number of liveborns with Down syndrome in the monitored California counties. The effect was greatest for whites and least for Hispanics, with results indicating considerable variation in the use of prenatal diagnostic services among racial/ethnic groups. Estimates of adjusted total prevalence and reduction in live births with Down syndrome in this study should be considered minimal because of some underascertainment of prenatally diagnosed cases. Am J Epidemiol 1997; 145:134–47.

age factors; Down syndrome; maternal age; prenatal diagnosis; racial stocks; sex ratio

Because of the high prevalence and serious health consequences of Down syndrome, many studies have been conducted throughout the world to increase understanding of the epidemiology of this anomaly. The relation of advanced maternal age to an increased risk of Down syndrome has been well established, but the associations of other risk factors, if any, have not been confirmed. Although some studies have addressed the role of race/ethnicity and its association with this anomaly, there is little conclusive evidence of racial differences in the risk of Down syndrome (1, 2). In the United States, a relation with race was recently described in two studies which showed different maternal age-specific rates between whites and persons of other races (Huether et al., University of Cincinnati, unpublished manuscript) and between Latinos and non-Latinos (3). Factors shown to be associated with the prevalence of Down syndrome in a population independently of maternal risk rates are 1) the maternal age structure of the population and 2) the use of prenatal diagnosis followed by elective abortion of affected fetuses (4).

Attempts to understand the etiology and natural history of Down syndrome have included efforts to
analyze sex ratios among affected liveborns, fetuses, and abortuses within populations in relation to biological factors. At present, it is well accepted that the number of males exceeds the number of females among liveborn infants with Down syndrome, although there is no known explanation for this phenomenon. Race has been shown to be an important factor associated with the sex ratio in all live births (5); yet, to our knowledge, no studies have been conducted that directly discussed the possible relation between race and sex ratios relative to Down syndrome.

Surveillance systems and registries of birth defects that include such anomalies as Down syndrome and that provide population-based data are critical resources in epidemiologic studies. With the introduction of prenatal diagnosis in the early 1970s and the opportunity to abort affected fetuses, there arose a need for additional data regarding the impact of this diagnostic information and consequent decision-making on the prevalence of Down syndrome and other birth defects. In the United States, there are only a few reliable and well established monitoring programs that provide both of the essential data sets needed for the continuing study of the epidemiology of Down syndrome. Two of these sources are the California Birth Defects Monitoring Program (CBDMP), a large, active live birth registry, and the Genetic Disease Branch of the California Department of Health Services, which maintains a statewide registry of prenatally diagnosed fetuses affected with chromosomal anomalies. These resources provide an opportunity to study the total prevalence of Down syndrome, including electively terminated pregnancies, and the impact of prenatal diagnosis in a US population.

This study examined several epidemiologic aspects of Down syndrome in a California population for the period 1989-1991. Because of the state's large and diverse population, the California data sets were stratified into five racial/ethnic categories. The primary objectives of this study were: 1) to calculate adjusted prevalence rates and quinquennial maternal age-specific risk rates of Down syndrome after adjusting for elective abortion of prenatally diagnosed fetuses; 2) to estimate the impact of prenatal diagnosis and subsequent elective abortion of diagnosed fetuses on the observed prevalence of Down syndrome among liveborn infants; and 3) to examine sex ratios among liveborns and fetuses with Down syndrome.

**MATERIALS AND METHODS**

**Live births and prenatally diagnosed cases**

The CBDMP, which maintains a population-based, active surveillance registry of live births and stillbirths with structural congenital anomalies in selected California counties, provided the data on liveborn infants with Down syndrome used for this study. In 1989, all California counties except Los Angeles County were monitored by the CBDMP. A reduced number of counties were monitored in 1990 and 1991, but Los Angeles County was included in both of these years. Cases of Down syndrome were identified by data collection specialists who abstracted information from the records of hospitals and genetic centers. Over 99 percent of these cases were confirmed by cytogenetic analysis. The data set was restricted to recorded resident live births occurring within monitored counties.

Five racial categories were used to classify cases: Hispanic white, non-Hispanic white, black, Asian, and other. Although Hispanics are technically an ethnic group, the term "race" was used to describe these five groups within the population. Race was assigned according to the mother's ethnicity, information obtained from medical records, and California vital statistics. Mexican, Puerto Rican, Cuban, and South American mothers were considered Hispanic. Whites consisted of non-Hispanic Caucasians, and blacks were persons of African ancestry. Asians included mothers who were Chinese, Japanese, Korean, Vietnamese, or Cambodian. The "other" category consisted of Filipinos, Hawaiians, and American Indians. The exact criteria applied to the racial assignment of individuals are unknown, and it is possible that these racial designations reflect different socioeconomic classes as well as subpopulations with different heritages.

The Genetic Disease Branch (GDB) of California's Department of Health Services collects information on cytogenetically diagnosed cases of Down syndrome, and it was the primary source of data for prenatal cases. All state-approved prenatal diagnosis centers in California are required to report information on diagnosed chromosomal anomalies to the GDB, including the mother's county of residence and her estimated date of confinement. A prenatal case of Down syndrome was included in this study only if the mother lived in a county monitored by the CBDMP and if her estimated date of confinement fell within the time period of monitoring. This restriction of the prenatal cases permitted an appropriate comparison with the live birth cases collected by the CBDMP. All prenatal cases were classified into the same five racial categories as the live birth cases.

Many live birth and prenatal cases of Down syndrome were ascertained by both the CBDMP and the GDB. This duplication afforded us a means of validating the accuracy of information on individual cases...
and of evaluating case ascertainment within each data set.

Demographic information on live births was provided by the Vital Statistics Division of the California state health department. These data were used as denominators to calculate prevalence rates of live births with Down syndrome.

**Cases of Down syndrome with unknown race or maternal age**

Of the 998 observed live birth cases of Down syndrome in 1989–1991, 26 cases did not have information available on the mother’s age, race, or both. Those cases were arbitrarily assigned a race or maternal age according to the maternal age and race proportions of the known cases, and totals were then rounded to the nearest whole number.

Of the 475 electively aborted fetuses prenatally diagnosed with Down syndrome in 1989–1991, 9.3 percent (44) of the cases did not have a recorded race, 2.7 percent (13) did not have a recorded maternal age, and 1.2 percent (6) had neither race nor maternal age recorded. Because exclusion of all of those cases would have resulted in a substantial underestimate of the impact of prenatal diagnosis on the prevalence of Down syndrome in this population, the cases with only an unknown race or an unknown maternal age were proportionally assigned a race or maternal age. Cases with both unknown race and unknown maternal age were excluded from all analyses. Of the 44 cases with unknown race, 28 were from 1989, 7 were from 1990, and 9 were from 1991. The 16 cases from 1990 and 1991 were assigned a race based on the known maternal age for each case and the racial proportion of women of that age for each year. The 28 cases of unknown race from 1989 represented such a large percentage (15.9 percent) of the total number of elective abortions for that year that a proportionalized assignment of race did not seem appropriate. Therefore, neither the maternal age-specific risk rates nor the impact of prenatal diagnosis was analyzed among racial categories for 1989. The 13 cases with an unknown maternal age were assigned a maternal age according to the known race of each case and the distribution of maternal ages within that racial group for each year. Total numbers of cases were not rounded to the nearest whole number because these values were further adjusted by the survival probability term discussed below. For this reason, some values shown in the tables contain fractions of cases. For the sex-ratio analysis in which race and maternal age were considered, only cases with a known race and maternal age were included.

**Calculation of prevalence rates adjusted for elective terminations and percent reduction in live births with Down syndrome**

Most prenatal cases of Down syndrome were detected through amniocentesis, although a small percentage (approximately 10 percent) were detected using chorionic villus sampling. In comparison with a fetus that has a normal karyotype, a fetus with Down syndrome detected through amniocentesis has an estimated 74 percent chance of surviving to birth if the mother chooses to continue the pregnancy (6). Therefore, the number of fetuses with prenatally detected Down syndrome that were electively aborted was multiplied by the survival probability term 0.74. This value was then added to the number of liveborn infants with Down syndrome to obtain the number of live births that would have been expected in the absence of prenatal diagnosis and elective abortion of the affected fetuses. The “adjusted total prevalence rate” was then calculated by dividing this adjusted total number of cases by the sum of all recorded live births plus the number of live births expected among electively aborted fetuses with Down syndrome. The phrases “adjusted total prevalence rate” and “adjusted total cases” are used throughout this paper to refer to total numbers of live births with Down syndrome that include the number of terminated pregnancies adjusted by the survival probability term 0.74. The phrases “observed live birth prevalence rate” and “observed live births with Down syndrome” refer to values that do not include the terminated pregnancies. The percent reduction in live births with Down syndrome attributable to prenatal diagnosis followed by elective abortion of affected fetuses was calculated by dividing the adjusted number of electively aborted fetuses by the adjusted total number of cases.

**Statistical methods**

Multiple logistic regression models (7) were used to relate risk rates of Down syndrome to the independent variables of year of birth, mother’s age and race, and sex. All independent variables were categorical. Chunk tests, in which differences in the deviances of models were calculated, were used to test the significance of multiple levels of the categorical variables. These tests are equivalent to likelihood ratio tests, which measure the strength of the association between individual independent variables and the dependent variable (prevalence of Down syndrome) after controlling for other variables in the model. Interactions of categorical variables were assessed using homogeneity of odds ratio tests in which deviances of test models and fully saturated models were compared. If signifi-
cant differences were observed, a closer examination of the significance of individual comparisons within the model was accomplished by performing a Bonferroni adjustment for multiple comparisons. Similar methods were used to relate sex ratios with categorical variables. Heterogeneity chi-squared tests were used to compare the sex ratios of prenatally diagnosed cases of Down syndrome for several categories of pregnancy outcome.

RESULTS

In the 1989–1991 California data set, a total of 998 live births with Down syndrome and 469 electively aborted fetuses with Down syndrome were ascertained. There were 531 Down syndrome cases diagnosed prenatally. Of those, 86 percent were diagnosed via amniocenteses, 10 percent by chorionic villus sampling, and the remaining 4 percent by unknown methods. Eighty-eight percent (n = 469) of these pregnancies were electively terminated, and 12 percent (n = 62) were continued. Twenty-four percent (n = 15) of the continued pregnancies resulted in spontaneous abortions and 76 percent (n = 47) resulted in live births, which accounted for 5 percent of all live births with Down syndrome. Four percent (n = 43) of the live birth cases were translocations, and 3 percent (n = 29) were mosaics. Among prenatally diagnosed cases in which the pregnancy was electively terminated, less than 1 percent (n = 4) were identified as translocations, and 3 percent (n = 13) were mosaics.

Prevalence rates and maternal age-specific risk rates of Down syndrome

Table 1 displays the adjusted total number of cases of Down syndrome and the live birth denominators for 1989–1991 used in calculating the adjusted total prevalence rates and quinquennial maternal age-specific risk rates. Adjusted total prevalence rates for 1989, 1990, and 1991 were 1.35, 1.65, and 1.66 per 1,000 live births, respectively. There was a statistically significant association of year of birth with maternal age-specific risk rates of Down syndrome ($\chi^2 = 8.96$, 2 df; $p = 0.01$). The maternal age-specific risk rates for 1989 were different from rates for 1990 (Bonferroni value; $p = 0.03$) and also different from rates for 1991 (Bonferroni value; $p = 0.04$); however, no differences were found between 1990 rates and 1991 rates (Bonferroni value; $p > 0.90$). These differences were suspected to be the results of variation in maternal age structures within the 5-year quinquennial categories and variation in the racial structure of the populations included in the counties monitored in 1989 versus those monitored in 1990 and 1991.
fore, the data set was reduced to include only the 12 counties monitored during all 3 years of the study (table 2). The adjusted total prevalence rates for 1989, 1990, and 1991 were 1.48, 1.74, and 1.69 per 1,000 live births, respectively. No association of year of birth with maternal age-specific risk rates was detected ($\chi^2 = 1.79, 2 \text{ df}; p = 0.41$), although the adjusted total prevalence for 1989 was still lower than that for 1990 and 1991.

Because the 1990 and 1991 data for all monitored counties were homogeneous, they were combined and stratified by race. The 1989 data were not included in the racial comparison because of the incompleteness of information on race for the fetal cases of Down syndrome. Adjusted total numbers of Down syndrome cases and live births are shown by race in table 3. When all races and maternal ages were regressed together, no significant effect of race on the maternal age-specific risk rates of Down syndrome was found ($\chi^2 = 1.79, 2 \text{ df}; p = 0.41$). The effect of maternal age on the risk rates of Down syndrome was also determined to be homogeneous among races ($\chi^2 = 21.60, 24 \text{ df}; p = 0.60$). Pairwise regression of two races at a time revealed a significant difference among the maternal age-specific risk rates of Down syndrome for Hispanics and whites ($\chi^2 = 4.49, 1 \text{ df}; p = 0.034$). No other statistical differences were observed between any two races. These data suggest that the quinquennial maternal age-specific risk rates of Down syndrome among Hispanics and whites differed, yet this difference was not large enough to have a significant effect when all racial groups were considered together. Additionally, small sample sizes could have made it difficult to detect differences between races other than Hispanics and whites, both of which had large sample sizes.

In figure 1, the percentage of live births is plotted by single-year maternal age for each of the five racial categories shown in table 3. Similarities in live birth distributions are seen between Hispanics (- - -) and blacks (○ + -) and between whites (▲) and "others" (●). In general, Hispanics and blacks had a larger percentage of live births at earlier maternal ages than persons of the other races, whereas Asians (—) had a larger percentage of births to mothers aged 30 years or older. Although whites and "others" peaked at a younger age than Asians, the level and shape of the live birth distributions of these two races more closely resembled the Asian live birth distribution than those of blacks and Hispanics. Figure 1 helps to explain the variation in the adjusted total prevalence rates of Down syndrome among the races from 1.36 in blacks to 2.06 in Asians. The risk rates for Down syndrome increased dramatically with increasing maternal age;
therefore, those racial groups with more births at older maternal ages, such as Asians, exhibited higher rates of Down syndrome. Overall, the variation in adjusted total prevalence rates among racial groups shown in table 3 was primarily due to different maternal age structures, whereas the difference in prevalence rates between whites and Hispanics was additionally due to differences in maternal age-specific risk rates.

Reduction in live births with Down syndrome due to elective abortion of affected fetuses

The total reduction in live births of infants with Down syndrome due to elective abortion of diagnosed fetuses for 1989–1991 was 25.8 percent (table 4). Mothers aged ≥35 years had a total reduction of 49.1 percent, and those aged <35 years had a 6.6 percent reduction. The age category 40–44 years had the highest reduction (50.2 percent). Not surprisingly, there was a major increase in the effect of elective terminations between the age category 30–34 years and the 35- to 39-year category.

In table 5, the percent reduction in live births with Down syndrome for 1990–1991 is displayed by race and quinquennial maternal age. Whites had the highest total reduction (46.3 percent), whereas the lowest total reduction was seen in Hispanics (10.0 percent). Whites also had the highest reduction (70.6 percent) among mothers aged ≥35 years, while Asians had the second highest (50.8 percent). The observed live birth prevalence rates (terminated pregnancies not included) and adjusted total prevalence rates for each race in these 2 years are shown in figure 2. The differences between these prevalence rates within each race indicate the impact of prenatal diagnosis and elective abortion of fetuses affected with Down syndrome.

Figures 3–5 exhibit observed live birth prevalence rates and adjusted total live birth prevalence rates of Down syndrome plotted by single-year maternal age for 1990–1991. The differences in amplitude between these two prevalence rate curves show the reduction in live births with Down syndrome due to prenatal diagnosis and elective abortion of affected fetuses. The reduction for all races is shown in figure 3, with nearly all of the reduction occurring among women aged ≥35 years. Prevalence rates for whites and Hispanics are shown in figures 4 and 5, respectively. The reduction among Hispanic women was low in comparison with that among whites and among all races combined. The two racial categories shown in figures 4 and 5 represent the extremes of the observed reduction due to elective abortion of affected fetuses within a racial group.
Figure 1. Percentage of total live births with Down syndrome in all counties monitored by the California Birth Defects Monitoring Program, by race and maternal age, 1989-1991. Racial categories: Asian (—), black (+), Hispanic ( - - ), other (○), and white (▲).

Table 4. Percent reduction in live births of infants with Down syndrome in all counties monitored by the California Birth Defects Monitoring Program, by maternal age group, 1989-1991

<table>
<thead>
<tr>
<th>Maternal age (years)</th>
<th>Live birth cases</th>
<th>Elective abortuses</th>
<th>Total no. of cases*</th>
<th>% reduction</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;20</td>
<td>84</td>
<td>1.1</td>
<td>84.8</td>
<td>1.0</td>
</tr>
<tr>
<td>20-24</td>
<td>156</td>
<td>5.2</td>
<td>159.8</td>
<td>2.4</td>
</tr>
<tr>
<td>25-29</td>
<td>217</td>
<td>16.4</td>
<td>233.0</td>
<td>5.2</td>
</tr>
<tr>
<td>30-34</td>
<td>232</td>
<td>43.4</td>
<td>275.4</td>
<td>12.2</td>
</tr>
<tr>
<td>35-39</td>
<td>187</td>
<td>245.3</td>
<td>362.5</td>
<td>49.3</td>
</tr>
<tr>
<td>40-44</td>
<td>110</td>
<td>148.6</td>
<td>228.8</td>
<td>50.2</td>
</tr>
<tr>
<td>≥45</td>
<td>12</td>
<td>8.0</td>
<td>17.9</td>
<td>33.0</td>
</tr>
<tr>
<td>&lt;35</td>
<td>689</td>
<td>66.1</td>
<td>735.1</td>
<td>6.6</td>
</tr>
<tr>
<td>≥35</td>
<td>309</td>
<td>402.9</td>
<td>612.2</td>
<td>49.1</td>
</tr>
<tr>
<td>Total</td>
<td>998</td>
<td>489</td>
<td>1,345.0</td>
<td>25.8</td>
</tr>
</tbody>
</table>

*Observed Down syndrome live births plus electively aborted fetuses, adjusted for the probability of survival to live birth (0.74).

Sex ratios

Table 6 displays the male:female ratios for 1989-1991 by race and maternal age (<35 years vs. ≥35 years) for three pregnancy outcome categories: all live births, liveborn infants with Down syndrome, and all prenatally diagnosed fetuses with Down syndrome. A significant association between outcome category and sex ratio was observed after adjustment for other independent variables (χ² = 12.3, 2 df; p < 0.01). This effect was primarily due to overall differences between sex ratios among all live births and live births with Down syndrome (Bonferroni value; p = 0.01). The total sex ratio was higher among liveborns with Down syndrome than among all live births in every racial category except “other.”

Racial differences in sex ratios were found among all live births (χ² = 21.4, 4 df; p < 0.01) as well as among liveborns with Down syndrome (χ² = 13.4, 4 df; p = 0.01). Among all live births, total sex ratios ranged from 1.02 (blacks) to 1.07 (others). Racial variation in sex ratios among liveborns with Down syndrome was considerably greater, ranging from 0.76 (others) to 1.66 (Asians).

No statistically significant associations between maternal age and sex ratio were detected among races or between categories. Overall, a higher sex ratio was observed among infants or fetuses of older mothers (all races) than for those of younger mothers in all three categories, although no consistent patterns between the two maternal age categories were observed among races.

Sex ratios of prenatally diagnosed cases of Down syndrome for 1989-1991 are displayed according to pregnancy outcome in table 7. Although no significant differences in sex ratios were detected among these outcome categories, a comparison of these ratios is presented in the Discussion and was considered worthwhile because it aids in the understanding of sex selection, which may be occurring between the time of prenatal diagnosis and birth.

Discussion

Ascertainment of cases

Virtually all live births of infants with Down syndrome in the monitored region are considered to have been ascertained in the CBDMP data set. All cases
independently ascertained through the GDB data set were also found in the CBDMP registry, and numerous data sources are utilized by the professional staff of the CBDMP who actively abstract information from these sources. Even though essentially all live birth cases were karyotyped, eight false-positive cases (<1 percent of the total data set) were found and were ascribed to clerical errors. Many fetal cases of Down syndrome were present in both the CBDMP and GDB data sets, and this overlap provided us with a means of estimating the level of ascertainment of cases that were prenatally diagnosed and electively terminated. The CBDMP ascertained 36.2 percent of the elective abortuses in the GDB data set in 1990–1991, in addition to 11 cases not ascertained by the GDB. These data suggest that, in the remaining 63.8 percent of the GDB data set that did not overlap with the CBDMP data, an estimated 19 cases were not ascertained. After adjustment for the survival of Down syndrome fetuses (19 × 0.74), it was estimated that 14 cases were missed for the years 1990–1991. During this time period, a total of 220 adjusted fetal cases were ascertained; therefore, an estimated 6.0 percent (14 / (220 + 14)) of elective abortions may not have been accounted for in the calculations of total prevalence or in the reductions in live births with Down syndrome during 1990–1991. Thus, results presented in this study should be considered minimal estimates. The difference in levels of ascertainment between Down syndrome live births and electively terminated pregnancies was not unexpected, considering the fact that the CBDMP actively surveys for live births whereas the GDB passively obtains prenatal diagnosis data.

### Maternal age-specific risk rates and adjusted total prevalence rates

The differences in the maternal age-specific risk rates for 1989 versus those for 1990 and 1991 could be partially explained by the change in the monitored counties between 1989 and 1990, assuming that there existed varying maternal age structures within the quinquennial age categories or differences in the racial composition of the population among various counties. Although the significant differences between these maternal age-specific risk rates disappeared when the analysis was limited to only the 12 counties monitored during all 3 years, the adjusted total prevalence rate for 1989 still remained lower than that for 1990 and 1991. This lower rate could possibly be explained by underascertainment of affected fetuses in 1989, but the only known difference in the collection of cases was the change in the counties that were monitored. In a trend analysis of prevalence rates of Down syndrome in California, Hahn and Shaw (8)
found that a change in the data collection area within the California population was a confounder in determining prevalence rates of Down syndrome.

For all racial groups and monitored counties, the adjusted total prevalence rate of Down syndrome estimated in this study for 1989–1991 (1.53 per 1,000 live births) was somewhat higher than most rates reported in the literature. The most likely explanation is the change in the maternal age structure of the population between the current time period and that of the earlier studies, which can be attributed to the older maternal reproductive ages recently reached by the post-World War II "baby boomers." This trend is supported by Goodwin and Huether's (9) presentation of estimated and projected percentages of live births to women aged ≥35 years and overall incidences of Down syndrome for the United States for the years 1970–2002. In this study, the incidence in 1975 of 1.1 per 1,000 live births was projected to increase to 1.4 by 1991, based on the increase (from 4.6 percent to 7.2 percent) in births to women aged ≥35 years during this time period. Other possible explanations for the higher rate found in this study include underascertainment in earlier studies and inadequate data on prenatally diagnosed cases and elective termination of these pregnancies.

**Observed live birth prevalence rates**

Some epidemiologic studies of Down syndrome report only observed live birth prevalence rates, which do not include elective abortion of prenatally diagnosed fetuses in their calculations. In a recent 17-state population-based study of Down syndrome for 1983–1988, the Centers for Disease Control and Prevention (10) reported observed live birth prevalence rates for California Hispanics (1.34 per 1,000) and whites (0.94

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**FIGURE 2.** Prevalence rates (per 1,000 births) of observed live births (■) and adjusted total live births (●) with Down syndrome in all counties monitored by the California Birth Defects Monitoring Program, by race, 1990–1991.

**FIGURE 3.** Prevalence (per 1,000 births) of observed live births (■) and adjusted total live births (●) with Down syndrome for all racial groups, by maternal age, in all counties monitored by the California Birth Defects Monitoring Program, 1990–1991.
Associations between race and maternal age-specific risk rates

In the 13-county population monitored for 1990–1991, no significant differences in the quinquennial maternal age-specific risk rates of Down syndrome were found among the racial groups when the data were regressed together. Despite these similar risk rates, the actual adjusted total prevalences for the different races ranged from 1.36 in blacks to 2.06 in Asians, because of large differences in live birth distributions by maternal age among the races (figure 1). Regression analyses of two races at one time revealed a significant difference in quinquennial maternal age-specific risk rates only between Hispanics and whites. When these values were compared, Hispanics had higher rates in the age categories under 40 years, while whites had higher rates in the two oldest age categories (table 3).

Two recent studies from the United States have also assessed the relation between race and maternal age-specific risk rates of Down syndrome. For the purpose of comparison, risk rates from these studies are shown...
Wilson et al. (3) reported quinquennial maternal age-specific risk rates in Latinos from a 15-year study of Down syndrome live births in a Los Angeles hospital. Logistic regression analysis of these risk rates with those obtained for California Hispanics in the current study revealed no significant differences ($\chi^2 = 1.53, 1$ df; $p = 0.22$). Using data from 1970-1989 obtained in populations from Ohio and Atlanta, Georgia, Huether et al. (University of Cincinnati, unpublished manuscript) found significantly different single-year maternal age-specific risk rates between whites and persons of other races, with the latter category consisting primarily of blacks. The quinquennial maternal age-specific risk rates calculated for whites in the current California study were not significantly different from those of the whites in Ohio/Atlanta ($\chi^2 = 0.10, 1$ df; $p = 0.75$). Similarly, no significant differences were observed between the California blacks and the Ohio/Atlanta others ($\chi^2 = 2.23, 1$ df; $p = 0.14$). However, unlike the Ohio/Atlanta study, no significant differences were found in this study between the maternal age-specific risk rates of California whites and blacks ($\chi^2 = 0.41, 1$ df; $p = 0.52$). This difference could be attributed to the quinquennial maternal age comparison in our study versus single-year maternal age in Ohio/Atlanta, or to the small population size of blacks in our study.

Although significant differences were observed between the maternal age-specific risk rates of Hispanics and whites in the current study, there is no clear explanation for these results. One possibility is the existence of actual biologic differences in the rate of nondisjunction events or in the viability of affected fetuses between the two races. An environmental agent, possibly related to socioeconomic level, could have an effect, although past studies have not shown conclusive evidence of any causative environmental factors related to Down syndrome (2). No significant differences were observed between the maternal age-specific risk rates of any other racial groups in our study; however, it is possible that the small sample sizes of blacks, Asians, and others limited the interpretation of true racial effects on prevalence rates of Down syndrome.

**Impact of prenatal diagnosis on the prevalence of Down syndrome**

In this study, the total number of live births with Down syndrome was reduced 25.8 percent by the elective abortion of prenatally diagnosed fetuses. Without this reduction, the observed live birth prevalence of 1.13 would have been 1.53 (see tables 1 and 4). Similarly, Krivchenia et al. (11) found that the
Mikkelsen (12) estimated a 34.5 percent reduction in the probability of survival to live birth associated with the inclusion of prenatally diagnosed cases, adjusted for the probability of survival, increased the prevalence of Down syndrome and eliminated significant differences between observed and predicted total prevalences. In our study, the strikingly large difference in reduction between the maternal age categories 30–34 years (12.2 percent) and 35–39 years (49.3 percent), and more generally between the categories <35 (6.6 percent) and ≥35 (49.1 percent), reflects the high use of prenatal diagnostic services by women aged 35 years or older. Single-year maternal age data for all races (figure 3) indicated that this increased reduction for older women actually began at maternal age 34 years.

Several other studies have also shown a reduction in live births with Down syndrome due to prenatal diagnosis and elective abortion of affected fetuses. Mikkelsen (12) estimated a 34.5 percent reduction in live births with Down syndrome for 1989 among all maternal age categories in Denmark. For 1988–1989, Krivchenia et al. (11) found a 26 percent total reduction in metropolitan Atlanta and a 16 percent reduction in an Ohio population. In an Australian population, 41 percent of Down syndrome pregnancies were electively terminated among women aged ≥35 during 1980–1989 (13). The percent reductions found in the California counties are consistent with those reported in these recent studies. If California whites alone are considered, they have the highest reported birth reduction (46.3 percent for all maternal ages, 1990–1991). These high percentages are likely to be atypical of the entire US population, however, as evidenced by Ohio’s much lower rate.

Figure 2 and table 5 show that race is strongly associated with the reduction in Down syndrome live births through prenatal diagnosis. In 1990–1991, Hispanics showed a 10.0 percent reduction, in contrast to 46.3 percent for whites. The effects of these extremes are reflected in the live birth prevalence rates of Hispanics (1.44) and whites (0.93). After adjustment for elective termination of pregnancies, the total preva-

### TABLE 7. Sex ratios among prenatally diagnosed cases of Down syndrome according to pregnancy outcome (elective abortion, continued pregnancy, spontaneous abortion, or live birth) in all counties monitored by the California Birth Defects Monitoring Program, 1989–1991

<table>
<thead>
<tr>
<th>Maternal age (years)</th>
<th>All pregnancies</th>
<th>Elective abortions</th>
<th>Continued pregnancies</th>
<th>Live births</th>
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<tr>
<td></td>
<td>M*</td>
<td>F*</td>
<td>Ratio</td>
<td>M</td>
</tr>
<tr>
<td>&lt;35</td>
<td>43</td>
<td>42</td>
<td>1.02</td>
<td>31</td>
</tr>
<tr>
<td>≥35</td>
<td>234</td>
<td>188</td>
<td>1.18</td>
<td>212</td>
</tr>
<tr>
<td>Total</td>
<td>277</td>
<td>240</td>
<td>1.15</td>
<td>243</td>
</tr>
</tbody>
</table>

* M, no. of male cases; F, no. of female cases.

### TABLE 8. Adjusted total numbers of cases of Down syndrome* and quinquennial maternal age-specific risk rates for Latinos, whites, and blacks from various studies

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. of live births</td>
<td>Total no. of cases</td>
<td>Rate (per 1,000)</td>
</tr>
<tr>
<td>&lt;20</td>
<td>33,590</td>
<td>25.0</td>
<td>0.74</td>
</tr>
<tr>
<td>20–24</td>
<td>66,244</td>
<td>53.0</td>
<td>0.80</td>
</tr>
<tr>
<td>25–29</td>
<td>48,037</td>
<td>50.5</td>
<td>1.05</td>
</tr>
<tr>
<td>30–34</td>
<td>25,927</td>
<td>61.0</td>
<td>2.35</td>
</tr>
<tr>
<td>35–39</td>
<td>11,755</td>
<td>62.9</td>
<td>5.35</td>
</tr>
<tr>
<td>40–44</td>
<td>3,010</td>
<td>72.7</td>
<td>24.15</td>
</tr>
<tr>
<td>≥45</td>
<td>239</td>
<td>5.0</td>
<td>20.92</td>
</tr>
<tr>
<td>Total</td>
<td>188,802</td>
<td>330.1</td>
<td>1.75</td>
</tr>
</tbody>
</table>

* Observed Down syndrome live births plus electively aborted fetuses, adjusted for the probability of survival to live birth (0.74).
† Data from Wilson et al., 1992 (3). In this table, total cases and rates were calculated using the 0.74 probability term, although Wilson et al. originally used a probability term of 0.70.
‡ Data from Huether et al. (unpublished manuscript).
§ Data from Huether et al. (unpublished manuscript). The majority (>90%) of cases in the "other" racial category in this data set were in blacks.
llence rates of Down syndrome in these two racial
groups were similar (1.60 and 1.72, respectively), even
given their different maternal age structures and risk
rates (figure 2). Krivchenia et al. (11) reported a 36.4
percent reduction for whites in Atlanta during 1988–
1989, whereas the other racial category showed a
much lower reduction of 6.25 percent. During the
same time period, whites in Ohio exhibited a reduction
of 15.2 percent, and others showed a reduction of 21.5
percent (11). The observed reduction of affected live
births among California Hispanics in this study was
higher than the estimated 3 percent reduction observed
among the Los Angeles Latinos during 1974–1988
(3), but overall it was still very low in comparison with
other races in this study.

Explanations for differential use of prenatal diag-
nostic services among different races include 1) vary-
ing levels of awareness of risk factors associated with
Down syndrome; 2) variations in the availability, ac-
cessibility, and affordability of diagnostic services and
awareness of these services; and, probably most ap-
pliably, 3) differing views on elective termination of
a pregnancy. During the years of this study, the Cali-
ifornia Department of Health Services had an estab-
lished, statewide prenatal diagnosis program that of-
fered services at a network of approved centers.
Eligibility for this program included (but was not
limited to) advanced maternal age (≥35 years), a
family history of a genetic disorder, and having a
pregnancy in which one parent was a translocation
carrier. Additionally, a statewide maternal serum
α-fetoprotein screening program began in 1986 and
offered low-cost screening to all pregnant women in
California between 15 and 20 weeks’ gestation. Cer-
tainly, these programs have been instrumental in the
overall large reduction in live births of Down syn-
drome infants in California, but a better understanding
of the reasons for racial differences in the use of
prenatal diagnostic services in California would be
useful to health planners and educators.

Sex ratios

Comparisons of sex ratios for all live births, live-
borns with Down syndrome, and all fetuses with
Down syndrome revealed several statistically signifi-
cant differences. The overall sex ratio for liveborns
with Down syndrome (1.28) was significantly higher
than that observed for all live births in the same
monitored region (1.04). The sex ratio for all fetuses
with Down syndrome (1.15) was lower than that for
liveborns with Down syndrome, although no signifi-
cant difference was detected. Mikkelsen (12) found
sex ratios of 1.33 and 1.04 for live births and fetuses
with Down syndrome, respectively. In Sweden, Iselius
and Lindsten (14) reported a sex ratio of 1.27 for live
births with Down syndrome and 1.26 for electively
aborted affected fetuses. These results are similar to
those of this study, and they support the belief that
more males than females are born with Down syn-
drome, although, in a review of sex ratio estimates for
Down syndrome live births, Huether (15) found sev-
eral studies which reported sex ratios much closer to
those of live birth controls.

Previous studies have shown that race is an impor-
tant factor associated with sex ratios among all live
births. The significant racial effects found here for
both control and Down syndrome live births are con-
sistent with those reported in the literature (5, 16, 17).
The data from the current study suggest that whites,
Asians, and blacks have higher sex ratios than Hispan-
ics and others for live births with Down syndrome. A
statistical effect of maternal age was not observed,
although the total sex ratios for live births, live births
with Down syndrome, and elective abortuses are all
higher in older mothers. Data from Denmark (18) and
southwestern Ohio (Huether et al., University of Cinc-
ninnati, unpublished manuscript) have indicated a simi-
lar trend in the relation of maternal age to the sex
ratio.

These data may contribute to an increased under-
standing of the reasons for the greater number of male
liveborns with Down syndrome. A comparison of the
sex ratios for fetuses prenatally diagnosed with Down
syndrome and those for liveborns with Down syn-
drome (tables 6 and 7) suggests that, during the time
period between prenatal diagnosis and live birth, there
is selection favoring the survival of males. This selec-
tion for male fetuses is further supported by compar-
ison of the sex ratio among all prenatally diagnosed
cases in which pregnancy is continued (1.31) with that
among cases resulting in a live birth (1.42). There is a
hint of parental selection for males as well, as indi-
cated by a comparison of the sex ratio among cases
where pregnancy was electively terminated (1.14)
with that among prenatally diagnosed cases where
pregnancy was continued (1.31). These data provide
only a partial explanation for the greater proportion of
males born with Down syndrome, since they do not
explain the higher sex ratio for all fetuses diagnosed
prenatally.

Conclusions

This study demonstrates that prenatal diagnosis and
consequent termination of pregnancies with fetuses
affected by Down syndrome had a substantial impact
on the number of live births of infants with Down
syndrome in monitored counties of California for
1989–1991, and that the use of prenatal diagnostic
services varied greatly among racial subpopulations. Maternal age structures also differed among various racial groups and had a dramatic effect on the adjusted total prevalence rates of Down syndrome, with whites and Asians exhibiting especially high rates. Additionally, a racial effect on maternal age-specific risk rates of Down syndrome was found between whites and Hispanics. These findings indicate that both utilization of prenatal diagnosis and race/ethnicity should be considered in the prediction of future prevalence rates of Down syndrome and health planning in California.

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REFERENCES