OBJECTIVE — We sought to assess the long-term trends in the incidence of type 1 diabetes among non-Hispanic white and Hispanic youth aged 0–17 years from Colorado using data from the Colorado IDDM Study Registry (1978–1988) and SEARCH for Diabetes in Youth (2002–2004).

RESEARCH DESIGN AND METHODS — Cases of diabetes were ascertained through physician reporting and hospital databases. Type 1 diabetes was defined as use of insulin within 2 weeks from diagnosis. Completeness of ascertainment was estimated as 97%. Annual average incidence rates (per 100,000/year) and 95% CIs for the time periods were computed. Trends in incidence were assessed by Poisson regression.

RESULTS — The incidence of type 1 diabetes was 14.8 (95% CI 14.0–15.6) in 1978–1988 and 23.9 (22.2–25.6) in 2002–2004 for the state of Colorado (P < 0.0001). From 1978 to 2004, the incidence of type 1 diabetes increased by 2.3% (1.6–3.1) per year (P < 0.0001). The increase in incidence was significant for both non-Hispanic white (2.7% [95% CI 1.9–3.6] per year, P < 0.0001) and Hispanic youth (1.6% [0.2–3.1] per year, P = 0.013).

CONCLUSIONS — The incidence of type 1 diabetes has increased 1.6-fold among Colorado youth from 1978–1988 to 2002–2004, and both non-Hispanic-white and Hispanic white youth are affected by this trend.


The incidence of type 1 diabetes is increasing in many regions of the world (1–3). Most population-based registries have shown an increasing incidence of type 1 diabetes over time (2,4–12), whereas others have shown no trend (13–17). Some of the inconsistencies may be attributed to differences in ascertainment and inadequate sample size to detect statistically significant changes over time. Data among U.S. youth are limited. The three U.S. registries that have produced the most reliable estimates are the Allegheny County Registry, Pennsylvania (1965–1994) (9,18); the Philadelphia Registry, Pennsylvania (1985–1999) (19–21); and the Colorado IDDM Study (1978–1988) (17,22). These three studies showed similar overall incidence rates of type 1 diabetes in youth; however, the studies had inconsistent results regarding possible trends in the incidence of type 1 diabetes in trends. The Colorado IDDM Study showed stable rates over an 11-year period (1978–1988). The Philadelphia Registry showed a stable rate for both Hispanic and non-Hispanic whites from 1985 to 1999 and an increase in incidence for black children. The Allegheny Registry showed a stable rate from 1965 to 1985 and a modest increase (0.22 per 100,000/year) from 1985 to 1989, mainly accounted for by an increase among nonwhite adolescents.
The hospital systems included Children’s Hospital, large community hospitals throughout the state, and hospital systems such as Exempla and Centura hospitals. A more detailed description of the Colorado IDDM Registry (17,22) and SEARCH Study (23) have been previously published.

The following criteria were used to assess eligibility for inclusion in the present analysis: 1) physician diagnosis of diabetes, 2) aged 0–17 years at diagnosis in the years covered by the two registries (1978–1988 and 2002–2004), 3) residence in Colorado in the year of diagnosis, 4) non-Hispanic white or Hispanic origin, and 5) daily insulin injections within 2 weeks after diagnosis or a provider diagnosis of type 1 diabetes. Patients who were institutionalized were excluded. The SEARCH Study ascertained incident cases of diabetes for the entire state of Colorado for 2002–2004 and ascertained cases living in the Denver metropolitan area in 2001, including those diagnosed in the Denver metropolitan area during the period 1996–2001. The Denver metropolitan area eligible cases, newly diagnosed in 1996–2004 and residing in a seven-county region of Denver, were identified to assist in assessing temporal trends. The Denver metropolitan area accounts for 60% of all cases of type 1 diabetes identified in Colorado.

Race/ethnicity data were collected using self-reports with period-specific Census-based questions. Race/ethnicity was defined as either 1) non-Hispanic or Latino white, which included all individuals who self-reported race/ethnicity as white and non-Hispanic or Latino; or 2) Hispanic or Latino, which included individuals of “any race” and Hispanic or Latino descent. The Census questions were modified in 1980, 1990, and 2000 with the addition of an “other race” category in 1990 and a category designating “two or more races” in 2000. These changes did not affect how race/ethnicity was defined in our study. Race/ethnicity could not be determined for 34 of 1,317 (2.6%) case subjects in 1978–1988 and 9 of 755 (1.2%) in 2002–2004; these case subjects were excluded from the analyses.

All participants provided informed consent, and both the Colorado IDDM Registry and SEARCH Study were approved by the Colorado Multiple Institutional Review Board and other relevant institutional review boards throughout the state.

**Denominators**
The denominator estimates include civilian noninstitutionalized Colorado youth aged 0–17 years. Annual age-, sex-, and ethnic-specific denominators were calculated by age-group, sex, and race/ethnicity. Percent average annual change was calculated by age-group, sex, and ethnicity. All analyses were repeated for the Denver metropolitan area for the periods 1978–1988 and 1996–2004.

**Statistical analysis**
Completeness of case ascertainment was assessed by the capture-recapture method using a two-mode ascertainment model (provider versus hospital sources) (26,27). As described above, case subjects were identified from multiple sources. A source was defined as any location where cases were reported. Once matching to identify duplicate ascertainment was accomplished across sources, the sources were further grouped into two modes of ascertainment: providers and in-patient hospital system records. The capture-recapture method was used to estimate the size of the unknown total population of type 1 diabetic patients by capturing them in one mode and recapturing them in another mode(s). Based on the assumption that the probability of capturing cases in both modes would be equal to the probability of capturing cases in each mode, the number of missed cases could be estimated and the completeness assessed (28). The percent completeness of ascertainment was defined as the number of observed cases divided by the estimated number by capture-recapture methodology. Completeness of case ascertainment was defined as 96% in 1978–1988 and 97% in 2002–2004.

Annual incidence and average annual incidence rates for the two time periods (1978–1988 and 2002–2004) were calculated by age-group, sex, and ethnicity and expressed per 100,000 person-years at risk. Direct adjustment of the incidence rates by sex and ethnicity were performed using the 2000 U.S. Census as the standard population using the age-groups 0–4, 5–9, 10–14, and 15–17 years; 95% CIs for the incidence rates were calculated assuming a Poisson distribution (29). Incidence rates for the two periods (1978–1988 and 2002–2004) were compared by computing incidence rate ratios (IRRs) and CIs. Temporal trends in incidence were assessed by Poisson regression modeling overall, as well as stratified by age-group (0–4, 5–9, 10–14, and 15–17 years), sex, and race/ethnicity. Percent average annual change was calculated by age-group, sex, and ethnicity. All analyses were repeated for the Denver metropolitan area for the periods 1978–1988 and 1996–2004.

**RESULTS**
A total of 1,281 youth with type 1 diabetes aged 0–17 years were diagnosed in 1978–1988. A total of 746 youth with type 1 diabetes were diagnosed in 2002–2004 in Colorado, whereas 1,097 youth were diagnosed in 1996–2004 in the Denver metropolitan area. Completeness of ascertainment was estimated as follows: non-Hispanic white, 96% for period I and 97% for period II; Hispanics, 95% for period I and 96% for period II.

Table 1 shows age-group–, sex–, and race/ethnic-specific incidence rates for each time period (period I, 1978–1988; period II, 2002–2004). The overall incidence of type 1 diabetes in Colorado was 14.8/100,000 per year (14.0–15.6) in 1978–1988 and 23.9/100,000 per year (22.2–25.6) in 2002–2004. This represents a 1.6-fold increase (IRR 1.6 [95% CI 1.46–1.74]). No significant differences by sex, race/ethnicity, age-group, and geography between the two time periods were found. The period II to period I IRRs were similar for non-Hispanic white (1.8 [1.6–1.9]) and Hispanic (1.4 [1.1–1.8]) youth and for male (1.6 [1.4–1.8]) and female (1.6 [1.4–1.9]) subjects. Although the difference failed to reach the nominal level of statistical significance (P = 0.058), youth aged 0–4 years had a somewhat greater increase in incidence from period I to period II (1.96 [1.6–2.4]) compared with the other age-groups (5–9 years, 1.6 [1.3–1.8]; 10–14 years, 1.5 [1.3–1.7]; and 15–17 years, 1.6 [1.2–2.1]). Non-Hispanic white female subjects were at a lower risk compared with non-Hispanic white male subjects in both periods (period I, 0.9 [0.8–1.0]; period II, 0.9 [0.8–1.0]). Hispanic female subjects were at slightly higher risk compared with Hispanic male subjects in period I (1.4 [1.0–2.0]), but no significant differ-
Figure 1 shows the temporal trends in the incidence of type 1 diabetes by ethnicity for both the entire state of Colorado (A) and the Denver metropolitan area (B). Overall, the incidence of type 1 diabetes increased similarly in Colorado (2.3% [95% CI 1.6–3.1] per year) and in the Denver area (2.5% [2.0–2.9] per year). There was a 2.7% annual increase in type 1 diabetes incidence for the non-Hispanic white youth (P < 0.0001) and an annual increase of 1.6% (P = 0.013) for Hispanic youth residing in Colorado. The trend appeared steeper for non-Hispanic white subjects compared with Hispanics; however, the slopes were not significantly different (P = 0.27 for the interaction between ethnicity and time), perhaps due to lack of power. Similar results were noted for the Denver metropolitan area (non-Hispanic white, 2.4% increase per year, P < 0.0001; Hispanic, 1.7% per year, P = 0.022).

Figure 2 shows the temporal trends in the incidence of type 1 diabetes among Colorado youth by sex and ethnicity. Overall, there was a significant and similar increase for both male and female subjects: male, 2.4% (95% CI 1.3–3.4) per year; female, 2.2% (1.1–3.4) per year. The increasing trend was significant for non-Hispanic white male (2.7% [1.6–3.7] per year), non-Hispanic white female (2.8% [1.4–4.1]), and Hispanic male (2.8% [0.6–5.1]) subjects but not for Hispanic female subjects (0.46% [−1.9 to 2.8] per year).

The average annual percent increase by age-group was also estimated. The 0- to 4-year age-group had the largest annual increase (3.5% [95% CI 2.1–4.9] per year), with the other age-groups having a similar increase (5–9 years, 2.2% [1.0–3.5] per year; 10–14 years, 1.8% [1.0–2.7] per year; and 15–17 years, 2.1% [0.5–3.7] per year; P = 0.059 for age-group 0–4 years vs. other age-groups).

**CONCLUSIONS**— We found that type 1 diabetes is increasing in Colorado youth aged 0–17 years at an average rate of 2.3% per year (95% CI 1.6–3.1). The overall incidence of type 1 diabetes in Colorado has significantly increased from 14.8/100,000 per year to 23.9/100,000 per year over the last 27 years.

A systematic review of incidence data from worldwide studies ranging from 8 to 32 years over the period 1960–1996 showed that a significant rise in incidence was recorded for 24 of 37 longitudinal studies, with a similar trend in an additional 12 (2). The EURODIAB Study, a large European survey for the period 1989–1998, showed a 3.2% (95% CI 2.7–3.7) annual increase. Our data show a similar, although slightly lower, average annual increase rate compared with the reported international average annual increase (31).

The U.S. stood apart from other parts of the world with the Colorado IDDM Registry reporting a stable incidence of childhood type 1 diabetes over much of the previous two decades (1978–1988) (32). A rapid increase was noted in the Allegheny County population over the period 1985–1989, which reflected a more recent increase among nonwhite adolescents (9). Additional reports that the incidence of childhood type 1 diabetes may be increasing in the U.S. come from registries in Philadelphia (20,21) and Chicago (33), which reported increases among African Americans and individuals from Hawaii, which reported a fourfold overall increase between 1980 and 1989 (34). In comparing worldwide reports on type 1 diabetes incidence, the current rates range from 0.1/100,000 per year in China to 40.2/100,000 per year in Finland (1,35). In Colorado, the current incidence rates fall approximately in the middle. Compared with the most recent U.S. reports from the Allegheny County Registry (16.7/100,000 per year) for 1990–1994 (18) and the Philadelphia Registry (14.8/100,000 per year) for 1995–1999 (21), the current Colorado
incidence rate is substantially higher (23.9/100,000 per year) for 2002–2004.

The major strength of this study is the availability of long-term data on type 1 diabetes incidence collected in the same geographic area, using similar case ascertainment methods and identical case definitions. While in the first time period case ascertainment relied heavily on hospitals and smaller endocrine and nonendocrine specialty practices, the later period ascertainment was mostly based on large pediatric endocrine practices (Barbara Davis Center, Pediatric Endocrine Associates) and less on hospital sources. This was mainly due to the changes in health care systems for childhood diabetes in Colorado (i.e., less youth with diabetes are now hospitalized at diagnosis) but also to recent U.S. laws concerning privacy and confidentiality (36). Of all cases ascertained, the hospital-based mode of ascertainment identified 84% in 1978–1988 and 26% in 2002–2004, whereas the provider-based mode identified 79 and 94%, respectively. Nevertheless, completeness of ascertainment was estimated to be ~97% for both periods included in this analysis, and it was similar for non-Hispanic white and Hispanic subjects.

The other strength is the inclusion of two racial/ethnic groups: non-Hispanic white and Hispanic children. While other U.S. population-based registries report a modest increase in the incidence of type 1 diabetes, mainly among older minority youth, this is the first U.S. data to demonstrate an increase among non-Hispanic white youth of similar pattern and magnitude to the European studies.

Different hypotheses have been proposed to explain the worldwide increase in type 1 diabetes incidence in youth. The “hygiene hypothesis” proposes that the decreasing early life exposure to infectious agents in Westernized societies has led to an impairment in the maturation of the immune system, thus permitting an increased occurrence of immune-mediated disorders, such as asthma and type 1 diabetes (37). The “accelerator” and the “overload” hypotheses both postulate that an increase in BMI in genetically susceptible individuals accelerates B-cell decline, leading to an early age at onset of type 1 diabetes (38–40). All these hypotheses require further testing.

Unlike other reports (9,18–21), the average annual increase reported here is slightly higher for non-Hispanic white compared with Hispanic youth (2.7 vs. 1.6%, P = 0.27). The increase in incidence was slightly higher among the 0- to 4-year age-group (3.5% [95% CI 2.1–4.9] per year). This finding is consistent with data from Europe where the increased incidence in children aged 0–4 years is 4.8% (3.8–5.9) pooled over 36 EURODIAB centers (39,41–43). The reason(s) for this rapid increase in young children is unclear. Several European studies (39,44,45) suggest that it might be due to a continuous decline in the age at onset of type 1 diabetes in conjunction with a more permissive early life environment (i.e., an environment that is more favorable to the development of diabetes) (31).

Our study has several limitations. First, there was a long period (from 1989 to 2001) during which incident cases with type 1 diabetes were not ascertained in the entire state of Colorado. Given this lack of data, we are unable to determine whether the increase was linear or nonlinear. This is especially important since the previous Colorado IDDM Registry showed no increase in incidence over the first 11 years of this analysis (1978–1988) (17); however, the model that best fit these data are linear. Moreover, the estimated annual average increase was similar for the entire state of Colorado and for the Denver metropolitan area for which additional years of data collection were available (from 1996 to 2001).

Misclassification of diabetes type is
25 Hispanic female subjects from Colorado with type 2 diabetes, aged 10–17 years at diagnosis, in 2002–2004, 6 (24%) had diabetes autoantibodies (either GAD65 or insulinoma-associated protein 2) measured as part of the SEARCH Study (unpublished results). Including the six possibly misclassified Hispanic female subjects in our type 1 diabetes incident case count did not significantly change the incidence trend, which suggests that the misclassification that exists in this study is minimal and does not substantially affect our findings.

The worldwide increase in the incidence of type 1 diabetes is worrisome. Active surveillance may help identify possible environmental determinants associated with diabetes over time. The ongoing Centers for Disease Control and Prevention–funded SEARCH for Diabetes in Youth Study (23) is a major effort in this direction. The current health information privacy laws in the U.S. are a major challenge to the development of population-based registries of chronic conditions, including childhood diabetes (49). It is, however, imperative that surveillance and tracking of this disease continue not only to understand its etiology, but also because of its increasing public health importance. The increasing risk of diabetes among U.S. youth leading to earlier morbidity and mortality supports the need for the development of a national diabetes registry.

Our data present strong evidence that type 1 diabetes is increasing among Colorado youth of both non-Hispanic white and Hispanic origin. This increase is similar in pattern and magnitude to the one reported over the last two decades by most European studies (1–3). Better surveillance systems for childhood diabetes are needed in the U.S. in order to understand the reasons for this increase and to develop successful preventive efforts.

Acknowledgments—The Colorado IDDM Registry and the SEARCH for Diabetes in Youth Study were funded by the Centers for Disease Control and Prevention and by the National Institutes of Health.

Parts of this study were presented in abstract form at the 66th Annual American Diabetes Association Scientific Sessions in Washington, DC, 9–13 June 2006.

We acknowledge the efforts of the physicians, clinics, and hospital staff involved in the collection of data for the Colorado IDDM Registry and the SEARCH Study.

Figure 2—Type 1 diabetes incidence in 0- to 17-year-old youth in Colorado by sex and ethnicity: non-Hispanic white (NHW) (A) and Hispanic (HISP) (B) subjects, 1978–1988 and 2002–2004.
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