Increasing Incidence of Type 1 Diabetes in 0- to 17-Year-Old Colorado Youth

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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 youth are affected by this trend.

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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 youth. 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. During this same time period, Europe, Japan, and New Zealand reported a 3–10% increase in the incidence of type 1 diabetes in children (5).

This study estimated long-term trends (1978–2004) in the incidence of type 1 diabetes in Colorado among 0- to 17-year-old Hispanic and non-Hispanic white youth by age-group, sex, and ethnicity.

RESEARCH DESIGN AND METHODS

Included in this analysis were all eligible individuals with new-onset physician-diagnosed type 1 diabetes who were identified through two population-based diabetes studies conducted in Colorado: the Colorado IDDM Registry and the SEARCH for Diabetes in Youth Study. The Colorado IDDM Registry was a statewide diabetes registry developed to ascertain all youth of non-Hispanic white and Hispanic origin with physician-diagnosed type 1 diabetes, aged 0–17 years at diagnosis, from 1 January 1978 to 31 December 1988 (17,22). SEARCH is a six-site, multiethnic, population-based observational study that ascertained all patients with physician-diagnosed diabetes who were aged 0–19 years on 31 December 2001, retrospectively, and all new cases of diabetes in youth aged 0–19 years from 1 January 2002 forward (23). As one of six clinical sites participating in the SEARCH Study, Colorado identified youth with prevalent diabetes in 2001 who resided in the Denver metropolitan area at diagnosis (seven counties covering 55% of the Colorado population) and is conducting ascertainment of cases newly diagnosed in 2002 and beyond in the entire state of Colorado. Ascertainment of incident cases is an ongoing SEARCH Study process.

The two registries utilized similar surveillance methods to ascertain youth with diabetes. The case ascertainment approach in both periods involved a network of providers and hospitals that referred cases to the study. The network of providers included large pediatric endocrine practices existent in both periods, such as the Barbara Davis Center for Childhood Diabetes, other specialty and primary care practices, Community Health Centers, and other providers and diabetes educators throughout the state.

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Abbreviations: IRR, incidence rate ratio.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

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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 linearly interpolated for the 1978–1988 period and projected for the 2002–2004 period from the 1980, 1990, and 2000 U.S. Census mid-year annual estimates. The ethnic-specific denominator estimates for 1978–1988 for the Denver metropolitan area were calculated by interpolation using Census-estimated population distributions for the seven counties by age-group and sex. The ethnic-specific denominator estimates for 1996–2004 were calculated by the U.S. Census Bureau using distributive cohort component methodology applying the above definition for race/ethnicity (24,25).

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 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. SAS version 9.1 (30) was used for all analyses.

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-

Table 1—*Age-specific incidence of type 1 diabetes by sex and race/ethnicity in 0- to 17-year-old Colorado youth, 1978–1988 and 2002–2004*

	Non-Hispanic white						Hispanic white					
	Female			Male			Female			Male		
	n	Rate	95% CI	*n*	Rate	95% CI	*n*	Rate	95% CI	*n*	Rate	95% CI
Period I (1978–1988)												
Age-group (years)												
0–4	78	7.9	3.5–15.2	117	11.2	5.8–19.3	8	3.6	0.10–19.0	13	5.6	0.44–22.5
5–9	167	18.7	10.8–29.8	189	20.0	12–31	27	12.3	2.5–34.8	9	4.0	0.15–19.7
10–14	220	23.4	14.6–35.1	229	23.1	14.5–34.5	37	17.8	4.9–44.2	28	13.4	2.9–37.3
15–17	51	8.3	2.9–18.4	88	13.4	6.1–25.0	10	8.1	0.38–37.5	10	8.1	0.38–37.4
Crude rate	516	15.0	13.7–16.3	623	17.1	15.8–18.5	82	10.6	8.5–13.1	60	7.6	5.8–9.7
Adjusted rate*	516	15.5	14.9–16.0	623	17.5	16.9–18.0	82	10.7	9.8–11.6	60	7.5	6.9–8.3
Period II (2002–2004)												
Age-group (years)												
0–4	51	17.4	10.4–27.1	70	22.7	14.7–33.2	9	7.9	2.0–20.4	16	10.7	4.0–22.5
5–9	93	32.4	22.3–45.2	100	32.9	21.9–46.7	18	14.9	5.9–30.1	16	11.6	4.3–24.5
10–14	117	36.7	26.4–49.4	125	37.0	26.9–49.4	20	17.5	7.3–34.3	24	20.4	9.3–38.1
15–17	32	16.7	8.6–28.7	45	22.0	12.6–35.0	4	6.5	0.6–25.0	6	9.5	1.6–29.2
Crude rate	293	26.9	23.9–30.1	340	29.4	24.3–35.6	51	12.5	9.3–16.2	62	13.5	10.5–17.2
Adjusted rate*	293	27.0	26.4–27.7	340	29.5	28.8–30.3	51	12.5	11.6–13.5	62	13.3	12.4–14.3
IRR (period II vs. I)		1.8	1.6–2.1		1.7	1.5–2.0		1.2	0.83–1.7		1.8	1.3–2.5

*Age-adjusted to U.S. 2000 standard population.

ences were noted in period II (0.86 [0.6–1.2]).

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

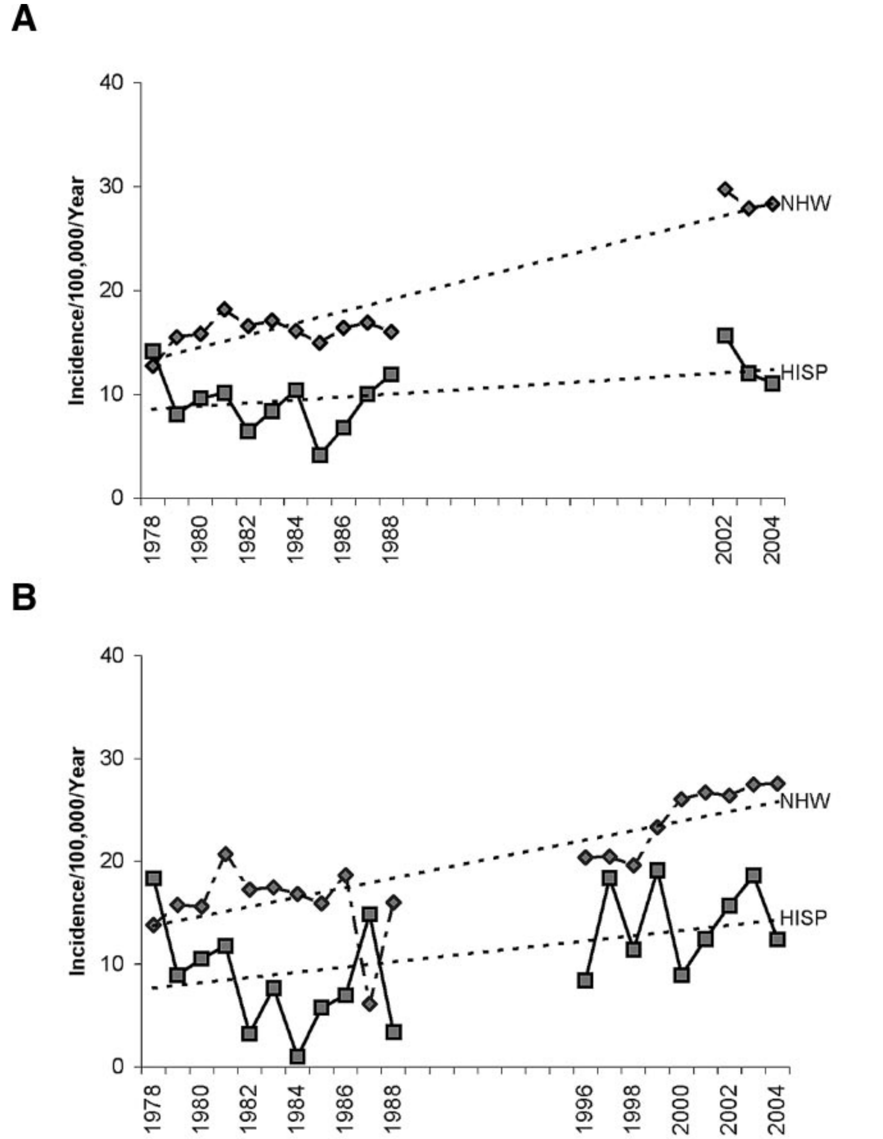

Figure 1—*Incidence of type 1 diabetes in Colorado 1978–1988 and 2002–2004 (*A*) and Denver metropolitan area youth 1978–1988 and 1996–2004 (*B*). HISP, Hispanic; NHW, non-Hispanic white.*

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 β-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

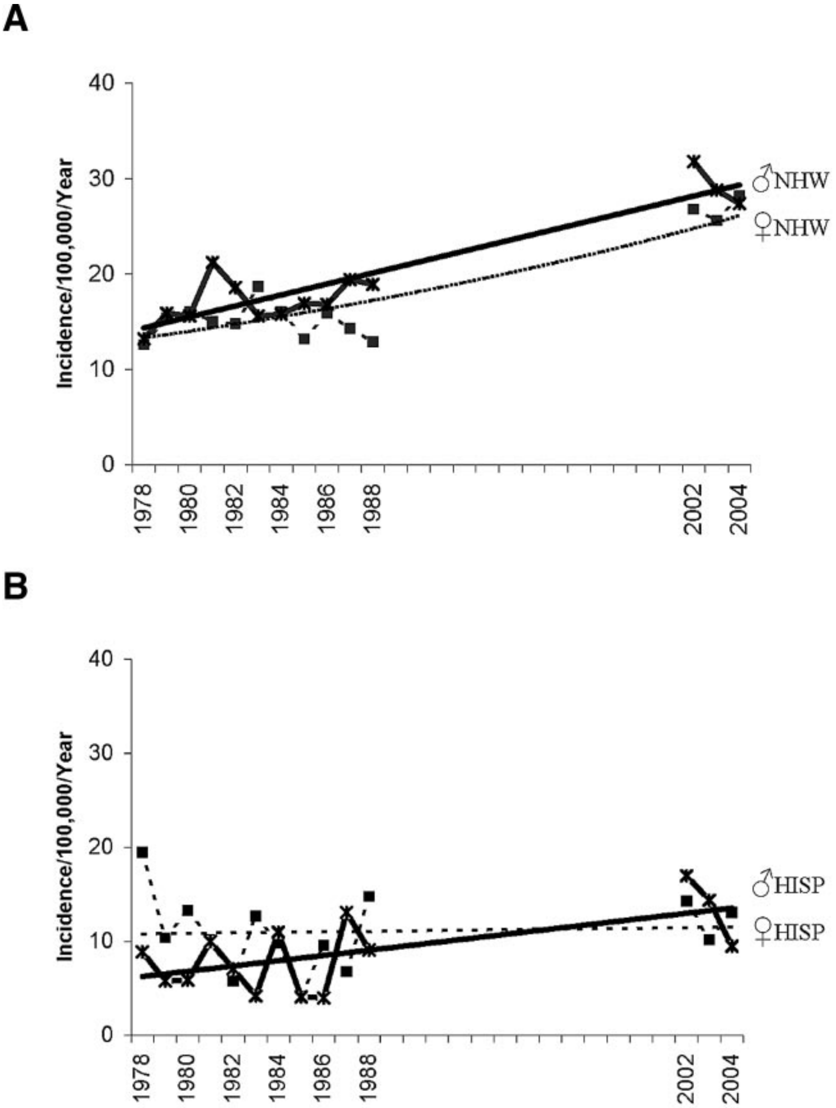

Figure 2—*Type 1 diabetes incidence in 0- to 17-year-old youth in Colorado by sex and ethnicity: non-Hispanic white (NHW) (*A*) and Hispanic (HISP) (*B*) subjects, 1978–1988 and 2002–2004.*

another potential limitation; however, the same definition of diabetes type was used over time. No measurements of diabetes autoantibodies were available for the period 1978–1988 (17). Of all Colorado cases with type 1 diabetes diagnosed between 2002 and 2004, 95% had positive diabetes autoantibodies measured as part of the SEARCH Study. In addition, the incidence of type 2 diabetes was estimated in Cincinnati, Ohio, to be very low before 1992 (0.7/100,000 per year) (46). This suggests that misclassification of diabetes type is unlikely to explain our findings. No increasing trend was noted for Hispanic female subjects (0.4% per year). The reasons for this finding are not entirely clear, but we need to acknowledge the small number of Hispanic female cases (approximately two per year). Type 2 diabetes has been reportedly increasing among Hispanic female adolescents in several clinic-based studies (47,48). Given the recent increased awareness of type 2 diabetes among minority youth, it is possible that some of the newly diagnosed Hispanic female subjects in the later time period were classified by their providers as having type 2 diabetes and not offered insulin treatment within 2 weeks from diagnosis. Such cases would be missed from our numerator in the later years, which could explain the lack of an increasing trend among Hispanic female subjects. We were able to assess this possible misclassification of type 2 diabetes in 2002–2004 cases, since the SEARCH Study collected biochemical markers. Of 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.

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References

1. Karvonen M, Viik-Kajander M, Moltchanova E, Libman I, LaPorte R, Tuomilehto J: Incidence of childhood type 1 diabetes worldwide: Diabetes Mondiale (DiaMond) Project Group. *Diabetes Care* 23: 1516–1526, 2000
2. Onkamo P, Vaananen S, Karvonen M, Tuomilehto J: Worldwide increase in incidence of type I diabetes: the analysis of the data on published incidence trends. *Diabetologia* 42:1395–1403, 1999
3. The DIAMOND Project Group: Incidence and trends of childhood type 1 diabetes worldwide 1990–1999. *Diabet Med* 23: 857–866, 2006
4. Rewers M, LaPorte R, Walczak M, Dmochowski K, Bogaczynska E: Apparent epidemic of insulin-dependent diabetes mellitus in midwestern Poland. *Diabetes* 36:106–113, 1987
5. Secular trends in incidence of childhood IDDM in 10 countries: Diabetes Epidemiology Research International Group. *Diabetes* 39:858–864, 1990
6. Nystrom L, Dahlquist G, Rewers M, Wall S: The Swedish childhood diabetes study: an analysis of the temporal variation in diabetes incidence 1978–1987. *Int J Epidemiol* 19:141–146, 1990
7. Tuomilehto J, Virtala E, Karvonen M, Lounamaa R, Pitkaniemi J, Reunanen A, Tuomilehto-Wolf E, Toivanen L: Increase in incidence of insulin-dependent diabetes mellitus among children in Finland. *Int J Epidemiol* 24:984–992, 1995
8. Tuomilehto J, Rewers M, Reunanen A, Lounamaa P, Lounamaa R, Tuomilehto-Wolf E, Akerblom HK: Increasing trend in type 1 (insulin-dependent) diabetes mellitus in childhood in Finland: analysis of age, calendar time and birth cohort effects during 1965 to 1984. *Diabetologia* 34: 282–287, 1991
9. Dokheel TM: An epidemic of childhood diabetes in the United States? Evidence from Allegheny County, Pennsylvania: Pittsburgh Diabetes Epidemiology Research Group. *Diabetes Care* 16:1606–1611, 1993
10. Variation and trends in incidence of childhood diabetes in Europe: EURODIAB ACE Study Group. *Lancet* 355:873–876, 2000
11. Joner G, Sovik O: Increasing incidence of diabetes mellitus in Norwegian children 0–14 years of age 1973–1982. *Diabetologia* 32:79–83, 1989
12. Songini M, Loche M, Stabilini M, Coppola A, Dessi G, Muntoni S, Balestrieri A, Bottazzo GF: The incidence of type 1 diabetes is rapidly increasing in Sardinian male army conscripts (Abstract). *Diabetologia* 35 (Suppl. 1):A25, 1992
13. Scott RS, Brown LJ, Darlow BA, Forbes LV, Moore MP: Temporal variation in incidence of IDDM in Canterbury, New Zealand. *Diabetes Care* 15:895–899, 1992
14. Bruno G, Merletti F, De Salvia A, Lezo A, Arcari R, Pagano G: Comparison of incidence of insulin-dependent diabetes mellitus in children and young adults in the Province of Turin, Italy, 1984–91: Piedmont Study Group for Diabetes Epidemiology. *Diabet Med* 14:964–969, 1997
15. Padaiga Z, Tuomilehto J, Karvonen M, Dahlquist G, Podar T, Adojaan B, Urbonaite B, Zalinkevicius R, Brigis G, Virtala E, Kohtamaki K, Cepaitis Z, Tuomilehto-Wolf E: Seasonal variation in the incidence of type 1 diabetes mellitus during 1983 to 1992 in the countries around the Baltic Sea. *Diabet Med* 16:736–743, 1999
16. LaPorte RE, Orchard TJ, Kuller LH, Wagener DK, Drash AL, Schneider BB, Fishbein HA: The Pittsburgh Insulin Dependent Diabetes Mellitus Registry: the relationship of insulin dependent diabetes mellitus incidence to social class. *Am J Epidemiol* 114:379–384, 1981
17. Kostraba JN, Gay EC, Cai Y, Cruickshanks KJ, Rewers MJ, Klingensmith GJ, Chase HP, Hamman RF: Incidence of insulin-dependent diabetes mellitus in Colorado. *Epidemiology* 3:232–238, 1992
18. Libman IM, LaPorte RE, Becker D, Dorman JS, Drash AL, Kuller L: Was there an epidemic of diabetes in nonwhite adolescents in Allegheny County, Pennsylvania? *Diabetes Care* 21:1278–1281, 1998
19. Lipman TH: The epidemiology of type I diabetes in children 0–14 yr of age in Philadelphia. *Diabetes Care* 16:922–925, 1993
20. Lipman TH, Chang Y, Murphy KM: The epidemiology of type 1 diabetes in children in Philadelphia 1990–1994: evidence of an epidemic. *Diabetes Care* 25: 1969–1975, 2002
21. Lipman TH, Jawad AF, Murphy KM, Tuttle A, Thompson RL, Ratcliffe SJ, Levitt Katz LE: Incidence of type 1 diabetes in Philadelphia is higher in black than white children from 1995 to 1999: epidemic or misclassification? *Diabetes Care* 29:2391–2395, 2006
22. Hamman RF, Gay EC, Cruickshanks KJ, Cook M, Lezotte DC, Klingensmith GJ, Chase HP: Colorado IDDM Registry: incidence and validation of IDDM in children aged 0–17 yr. *Diabetes Care* 13:499–506, 1990
23. SEARCH Study Group: SEARCH for Diabetes in Youth: a multicenter study of the prevalence, incidence and classification of diabetes mellitus in youth. *Control Clin Trials* 25:458–471, 2004
24. Analysis of data from the U.S. Census Bureau [article online], 2005. Available from www.aecf.org/kidscount/census. Accessed 15 November 2005
25. U.S. Census Bureau: *Estimates and Projections Area Methodology State Population Estimates by Age, Sex, Race and Hispanic Origin*. Washington, DC, U.S. Census Bureau, 2002
26. Verlato G, Muggeo M: Capture-recapture method in the epidemiology of type 2 diabetes: a contribution from the Verona Diabetes Study. *Diabetes Care* 23:759–764, 2000
27. Cochi SL, Edmonds LE, Dyer K, Greaves WL, Marks JS, Rovira EZ, Preblud SR, Orenstein WA: Congenital rubella syndrome in the United States, 1970–1985: on the verge of elimination. *Am J Epidemiol* 129:349–361, 1989
28. Tilling K: Capture-recapture methods: useful or misleading? *Int J Epidemiol* 30: 12–14, 2001
29. Rosner B: *Fundamentals of Biostatistics*. 5th ed. Boston, MA, Harvard University, Duxbury Press, 2000, p. 692
30. SAS/STAT software: changes and enhancements (release 9.1). Cary, NC, SAS Institute, 2001
31. Libman IM, LaPorte RE: Changing trends in epidemiology of type 1 diabetes mellitus throughout the world: how far have we come and where do we go from here. *Pediatr Diabetes* 6:119–121, 2005
32. LaPorte RE, Matsushima M, Chang YF: *Prevalence and Incidence of Insulin-Dependent Diabetes*. Bethesda, MD, National Institutes of Health, 1995 (NIH publ. no. 95-1468)
33. Lipton RB, Fivecoate JA: High risk of IDDM in African-American and Hispanic children in Chicago, 1985–1990. *Diabetes Care* 18:476–482, 1995
34. Patrick SL, Kadohiro JK, Waxman SH, Curb JD, Orchard TJ, Dorman JS, Kuller LH, LaPorte RE: IDDM incidence in a multiracial population: the Hawaii IDDM Registry, 1980–1990. *Diabetes Care* 20: 983–987, 1997
35. Patterson CC, Dahlquist G, Soltesz G, Green A: Is childhood-onset type I diabetes a wealth-related disease? An ecological analysis of European incidence rates. *Diabetologia* 44 (Suppl. 3):B9–B16, 2001
36. Health Insurance Portability and Accountability Act, 21 August 1996: Public Law 104–191, 104th Congress [online]. Available from http://aspe.hhs.gov/admnsimp/pl104191.htm. Accessed 3 November 2006
37. Gale EA: A missing link in the hygiene hypothesis? *Diabetologia* 45:588–594, 2002
38. Wilkin TJ: The accelerator hypothesis: weight gain as the missing link between type I and type II diabetes. *Diabetologia* 44:914–922, 2001
39. Pundziute-Lycka A, Dahlquist G, Nystrom L, Arnqvist H, Bjork E, Blohme G, Bolinder J, Eriksson JW, Sundkvist G, Ostman J: The incidence of type 1 diabetes has not increased but shifted to a younger age at diagnosis in the 0–34 years group in Sweden 1983 to 1998. *Diabetologia* 45:783–791, 2000
40. Dabelea D, D'Agostino RB Jr, Mayer-Davis EJ, Pettitt DJ, Imperatore G, Dolan LM,

Pihoker C, Hillier TA, Marcovina SM, Linder B, Ruggiero AM, Hamman RF: Testing the accelerator hypothesis: body size, beta-cell function, and age at onset of type 1 (autoimmune) diabetes. *Diabetes Care* 29:290–294, 2006
41. Karvonen M, Pitkaniemi J, Tuomilehto J: The onset age of type 1 diabetes in Finnish children has become younger: the Finnish Childhood Diabetes Registry Group. *Diabetes Care* 22:1066–1070, 1999
42. Schoenle EJ, Lang-Muritano M, Gschwend S, Laimbacher J, Mullis PE, Torresani T, Biason-Lauber A, Molinari L: Epidemiology of type I diabetes mellitus in Switzerland: steep rise in incidence in under 5 year old children in the past decade. *Diabetologia* 44:286–289, 2001
43. Green A, Patterson CC, the EURODIAB TIGER Study Group, Europe and Diabetes: Trends in the incidence of childhood-onset diabetes in Europe 1989–1998. *Diabetologia* 44 (Suppl. 3):B3–B8, 2001
44. EURODIAB Substudy 2 Study Group: Rapid early growth is associated with increased risk of childhood type 1 diabetes in various European populations. *Diabetes Care* 25:1755–1760, 2002
45. Hypponen E, Virtanen SM, Kenward MG, Knip M, Akerblom HK: Obesity, increased linear growth, and risk of type 1 diabetes in children. *Diabetes Care* 23: 1755–1760, 2000
46. Pinhas-Hamiel O, Dolan LM, Daniels SR, Standiford D, Khoury PR, Zeitler P: Increased incidence of non-insulin-dependent diabetes mellitus among adolescents. *J Pediatr* 128:608–615, 1996
47. Hamman RF, Marshall JA, Baxter J, Kahn LB, Mayer EJ, Orleans M, Murphy JR, Lezotte DC: Methods and prevalence of non-insulin-dependent diabetes mellitus in a biethnic Colorado population: the San Luis Valley Diabetes Study. *Am J Epidemiol* 129:295–311, 1989
48. Urrutia-Rojas X, Menchaca J: Prevalence of risk for type 2 diabetes in school children. *J Sch Health* 76:189–194, 2006
49. Ingelfinger JR, Drazen JM: Registry research and medical privacy. *N Engl J Med* 350:1452–1453, 2004