

Diabetes in Non-Hispanic White Youth

Prevalence, incidence, and clinical characteristics: the SEARCH for Diabetes in Youth Study

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reported by European countries. We believe efforts directed at improving the cardiometabolic and behavioral risk factor profiles in this population are warranted.

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OBJECTIVE — To investigate the incidence, prevalence, and clinical characteristics of diabetes among U.S. non-Hispanic white (NHW) youth.

RESEARCH DESIGN AND METHODS — Data from the SEARCH for Diabetes in Youth Study (SEARCH study), a multicenter study of diabetes among youth aged 0–19 years, were examined. Incidence rates were calculated per 100,000 person-years across 4 incident years (2002–2005), and prevalence in 2001 was calculated per 1,000 youths. Information obtained by questionnaire, physical examination, and blood and urine collection was analyzed to describe the characteristics of youth who completed an in-person visit.

RESULTS — The prevalence of type 1 diabetes (at ages 0–19 years) was 2.00/1,000, which was similar for male (2.02/1,000) and female (1.97/1,000) subjects. The incidence of type 1 diabetes was 23.6/100,000, slightly higher for male compared with female subjects (24.5 vs. 22.7 per 100,000, respectively, $P = 0.04$). Incidence rates of type 1 diabetes among youth aged 0–14 years in the SEARCH study are higher than all previously reported U.S. studies and many European studies. Few cases of type 2 diabetes in youth aged <10 years were found. The prevalence of type 2 diabetes (at ages 10–19 years) was 0.18/1,000, which is significantly higher for female compared with male subjects (0.22 vs. 0.15 per 1,000, $P = 0.01$). Incidence of type 2 diabetes was 3.7/100,000, with similar rates for female and male subjects (3.9 vs. 3.4 per 1,000, respectively, $P = 0.3$). High levels of abnormal cardiometabolic and behavioral risk factor profiles were common among youth with both type 1 and type 2 diabetes. For example, within each of four age-groups for youth with type 1 diabetes and two age-groups for youth with type 2 diabetes, >40% had elevated LDL cholesterol, and <3% of youth aged >10 years met current recommendations for intake of saturated fat. Among youth aged ≥ 15 years, 18% with type 1 and 26% with type 2 diabetes were current smokers.

CONCLUSIONS — The SEARCH study is one of the most comprehensive studies of diabetes in NHW youth. The incidence of type 1 diabetes in NHW youth in the U.S. is one of the highest in the world. While type 2 diabetes is still relatively rare, rates are several-fold higher than those

Approximately 20 million people in the U.S. have been diagnosed with diabetes (1), a figure driven primarily by type 2 diabetes in adults. In youth, the burden of diabetes is primarily due to type 1 diabetes; however, there is increasing concern regarding the diagnosis of type 2 diabetes at younger ages. The latest estimates indicate that for type 1 and type 2 diabetes combined, ~150,000 youth in the U.S. had diabetes in 2001 (2), and ~18,000 youth were diagnosed annually with diabetes in 2002–2003 (3).

International studies indicate that type 1 diabetes is most common among youth of northern European descent relative to other populations in the world. In the multinational World Health Organization Diabetes Mondiale (DiaMond) study, rates of type 1 diabetes among youth aged 0–14 years varied by 350-fold, from ~36/100,000 in Sardinia and Finland to 0.1/100,000 in China and Venezuela (4). In contrast, type 2 diabetes is more common among Hispanic, African American, and American Indian youth (5). In the U.S., studies of diabetes in youth are generally limited to those conducted in a single geographic location. Moreover, there are limited recent population-based data on the prevalence and incidence of type 1 diabetes among non-Hispanic white (NHW) subjects, while reports of type 2 diabetes among youth focus largely on data from members of ethnic minority groups. In general, these studies lack information regarding the clinical and behavioral characteristics of these populations, important factors in understanding this condition.

To address gaps in knowledge regarding diabetes among NHW youth in the U.S., this study uses data from the SEARCH for Diabetes in Youth Study (SEARCH study) to 1) provide the esti-

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mates of prevalence and incidence of diabetes among NHW youth in the U.S., overall and according to age and sex, and 2) describe the demographic, behavioral, clinical, and socioeconomic characteristics of this population.

RESEARCH DESIGN AND METHODS

The SEARCH study is a multicenter observational study that began conducting population-based ascertainment of cases of nongestational diabetes in youth aged <20 years beginning in 2001 and continuing through the present. Youth with diagnosed diabetes were identified in geographically defined populations in Ohio (eight urban and suburban counties encompassing and surrounding Cincinnati), Washington (five urban counties encompassing and surrounding Seattle), South Carolina, and Colorado (selected counties in 2001, all counties in subsequent years); among managed health care plan enrollees in Hawaii and southern California; and among Indian Health Service beneficiaries in four American Indian populations. Ascertained case subjects were contacted and asked to complete an initial patient survey, and subjects completing the initial patient survey were invited for an in-person visit, during which anthropometric and clinical data and samples were collected. A detailed description of the SEARCH study methods has been published elsewhere (6).

The SEARCH study sought to identify all existing (prevalent) cases of diabetes in 2001 and all newly diagnosed (incident) cases in subsequent calendar years. Diabetic cases were considered valid if diagnosed by a health care provider. Analyses herein include NHW cases prevalent in 2001 and incident cases for calendar years 2002–2005. Before implementation of the protocol, the study was reviewed and approved by the local institutional review board(s) that had jurisdiction over the local study population, and compliance with Health Insurance Portability and Accountability Act (HIPAA) regulations was ensured.

Data collection

Youth with diabetes or their parent/guardian were asked to complete a short initial survey that collected information on race and ethnicity as well as diabetes-related factors. Self-reported race and ethnicity were collected using 2000 U.S. Census questions (7).

Information about dietary intake,

physical activity, smoking and other health behaviors, and depressive symptoms was collected from participants aged ≥ 10 years. Dietary intake was assessed by a food frequency instrument modified for administration in youth and designed to capture regionally and culturally specific foods in the SEARCH study population, as previously described (8). Physical activity questions were derived from the Youth Risk Behavioral Surveillance System questionnaire (9). Depressive symptoms were assessed using the Center for Epidemiologic Studies–Depression Scale score, as previously reported (10,11).

For all participants, blood was drawn at the study visit for measurement of diabetes autoantibodies, A1C, fasting glucose, C-peptides, and lipids. A spot urine was also collected for measurement of urinary albumin. Specific laboratory methods for these tests have been previously described (6). The inter- and intra-assay variation for these measures are as follows: cholesterol 1.6 and 0.6%, C-peptides 3.1 and 1.4%, glucose 1.4 and 0.7%, GHb 0.7 and 0.5%, HDL 1.8 and 0.9%, creatinine 4.3 and 0.7%, triglycerides 1.8 and 1.0%, and urine albumin 3.8 and 2.9%, respectively.

For youth aged ≥ 3 years, a brief physical examination included height, weight, waist circumference, evaluation for acanthosis nigricans, and measurement of systolic and diastolic blood pressure (6). All data collection procedures were conducted following standardized procedures for training and certification on the study protocol. Training and data collection certification is repeated annually, and selected measures are evaluated for consistency following duplicate measurement quality-control procedures.

Categorization of key variables

Diabetes type was reported by the health care professional or abstracted from the medical records as type 1, type 1a, type 1b, type 2, maturity-onset diabetes of the young, hybrid, or other type. For this report, we have restricted our analyses to youth with type 1 diabetes (including type 1a and type 1b) or type 2 diabetes. Case subjects with maturity-onset diabetes of the young, hybrid, other types, or missing type were excluded (2.5% of registered case subjects).

Race/ethnicity was categorized somewhat differently for the prevalence and incidence estimates using all registered youth and for the analysis of respondent characteristics, which was based on the

subset of youth who had a study visit. For both analyses, all participants who reported “Hispanic” ethnicity were categorized as “Hispanic,” regardless of their responses to race questions. For the prevalence and incidence estimates, participants with multiple race categories were race bridged using methods developed by the National Center for Health Statistics (12). Participants with missing race and ethnicity data or who were classified as “other race” were geocoded (7.6% of registered case subjects were either geocoded or race bridged). For analyses of characteristics of youth with diabetes among the non-Hispanic participants, those who reported more than one race were placed into a single race category using the plurality approach. Subjects who could not be classified to one race group using the plurality approach (0.5% of study visit case subjects) and those with missing data (0.02% of study visit case subjects) were classified as “other race/ethnicity” and “unknown race/ethnicity,” respectively, and were excluded.

Estimation of prevalence

Methods for estimating diabetes prevalence in 2001 have been previously reported (2). Briefly, the numerator for the analysis included all NHW case subjects with nongestational diabetes prevalent in 2001 who were aged <20 years on 31 December 2001 and a resident of the defined population in 2001 (geographically based centers) or a member of the participating health plan in 2001 (membership-based centers). Age was based on the subject’s age on 31 December 2001. The study covered 2,025,426 NHW youth aged <20 years in 2001. The prevalence of diabetes among NHW youth was expressed as cases per 1,000 youth using data pooled across all SEARCH study centers, with 95% CIs calculated by using an inverted-score test from the binomial distribution (13).

Estimation of incidence rates

Annual incidence rates for 2002 and 2003 were published previously (3). Here, we present more detailed, race/ethnicity-specific incidence rates using diabetic case subjects ascertained with newly diagnosed diabetes over a 4-year period (2002–2005). Because the 2000 U.S. Census projections for youth residing in the participating areas were similar in 2002 and 2003 (–0.2% change overall), for simplicity, the 2002 denominator was multiplied by four and used as the total

denominator for case subjects ascertained over the 4-year period of 2002–2005. The study covered 11,856,800 NHW person-years at risk. Annual incidence rates were estimated per 100,000 youth, and 95% CIs were calculated by using an inverted-score test from the binomial distribution (13).

Clinical, behavioral, and socioeconomic characteristics

Weight and height were compared with U.S. standards to calculate normalized z scores (14). Youth with a BMI z score ≥ 95 th percentile were considered obese, 85–94.9th percentiles overweight, ≥ 5 th percentile to < 85 th percentile healthy weight, and < 5 th percentile underweight (15). Diabetes therapy was reported as being on insulin, metformin, both, or neither. Youth were defined as having diabetic ketoacidosis (DKA) at diagnosis (incident case subjects only) if they had at least one of the following noted in their medical record: 1) blood bicarbonate < 15 mmol/l or pH < 7.25 (venous) or < 7.30 (arterial or capillary), 2) ICD-9 code 250.1, or 3) diagnosis of DKA mentioned in the medical records (16). Family history of diabetes was defined as having a biological sibling, parent, or grandparent with diabetes. A1C was categorized using the American Diabetes Association guidelines as good (< 8.0), marginal (8.0–9.4), and poor (≥ 9.5) control (17). Glutamic acid decarboxylase (GAD65) levels ≥ 0.085 were considered positive (18). Waist circumference was measured using the National Health and Nutrition Examination Survey protocol (19), and high waist circumference was classified as ≥ 90 th percentile for age and sex (20). Hypertension was defined as systolic and/or diastolic blood pressure ≥ 95 th percentile for sex, age, and height (21). We also examined data on the prevalence of self-reported hypertension. Abnormal lipid values were defined as follows, using previously published treatment guidelines (22): triglycerides ≥ 110 mg/dl, HDL cholesterol ≤ 40 mg/dl, and LDL cholesterol ≥ 100 mg/dl. High albumin-to-creatinine ratio (ACR) was defined as having an ACR of ≥ 30 $\mu\text{g}/\text{mg}$ (23).

Smoking status was classified as never, former, and current. Participants were asked the average number of days they participate in physical activity in a typical week and were then divided into two categories: being physically active 0–2 days per week or 3–7 days per week. Two dietary variables, percent calories

from fat and saturated fat and the average number of servings of fruits and vegetables, were obtained by a food frequency questionnaire as previously described (8). A score of ≥ 24 on the Centers for Epidemiologic Study Depression Scale (10,11) was considered to indicate the presence of depressive symptoms. Annual family income was divided into four categories: $< \$25,000$, $\$25,000$ to $\$49,999$, $\$50,000$ to $\$74,999$, and $\geq \$75,000$. Parental education was classified as less than high school or at least a high school graduate and was based on the highest education of either parent. Insurance was classified for nonmembership sites as private, Medicaid or Medicare, other insurance, or none.

Statistical testing of the demographic, clinical, behavioral, and socioeconomic variables was conducted across subgroups aged 0–4, 5–9, 10–14, and ≥ 15 years for youth with type 1 diabetes and across the two older age-groups for type 2 diabetes. Comparisons were also made between youth with type 1 and type 2 diabetes. χ^2 tests, t tests, or ANOVA were conducted as appropriate. Mean fasting C-peptide is reported as adjusted for diabetes duration. Percent GAD65 positivity, high blood pressure, high triglycerides, low HDL cholesterol, high LDL cholesterol, apolipoprotein B (apoB), and high ACR are reported as unadjusted and adjusted for duration of diabetes. Linear or logistic regression was used to adjust for differences in diabetes duration between age categories for continuous and dichotomous outcomes, respectively. Given the descriptive and hypothesis-generating nature of these analyses, we retained use of the traditional α of 0.05 to determine statistical significance despite the number of comparisons made.

RESULTS — A total of 4,243 NHW youth aged < 20 years had diabetes in 2001, and an additional 3,041 youth were newly diagnosed in 2002–2005. A table in the online-only appendix (available at <http://care.diabetesjournals.org/cgi/content/full/dc09-S202/DC1>) shows details of numerators, denominators, and prevalence and incidence rates with 95% CIs, according to 5-year age-groups.

There were 4,045 type 1 and 198 type 2 diabetic prevalent case subjects in 2001. The prevalence of type 1 diabetes for youth aged 0–19 years was 2.00/1,000, which was similar for male (2.02/1,000) and female (1.97/1,000) subjects. The prevalence of type 2 diabetes among youth aged 10–19 years was 0.18, which

was significantly higher for female (0.22) compared with male (0.15, $P = 0.01$) subjects. A total of 2,800 type 1 incident case subjects were observed during the 4-year time period. The incidence of type 1 diabetes was 23.6/100,000, with the rates being slightly higher for male compared with female subjects (24.5/100,000 and 22.7/100,000, respectively, $P = 0.04$).

A total of 229 patients with type 2 diabetes in the 10–19 year age range were identified during the 4-year time period, and only 12 type 2 diabetic patients were diagnosed when aged < 10 years. The incidence of type 2 diabetes for youth aged 10–19 years was 3.7/100,000, with similar rates observed for female and male subjects (3.9/100,000 vs. 3.4/100,000, respectively, $P = 0.3$).

Figure 1 presents prevalence estimates (Fig. 1A) and annual incidence rates (Fig. 1B) of type 1 and type 2 diabetes, by single-year age-groups and sex. The prevalence of both type 1 and type 2 diabetes increased gradually with age. By age 19 years, the prevalence of type 1 diabetes was 3.33/1,000 for male subjects and 3.69/1,000 for female subjects and the prevalence of type 2 diabetes was 0.3/1,000 for both male and female subjects. Incidence of type 1 diabetes peaked at age 13 years for male subjects (39.07/100,000) and at age 11 years for female subjects (40.09/100,000). Rates of type 2 diabetes were highest for male subjects at age 14 years (6.63/100,000) and at age 15 years for female subjects (6.77/100,000).

Sociodemographic characteristics

For each of the four age-groups, $> 60\%$ of youth with type 1 diabetes were from families with $\geq \$50,000$ annual income and $> 78\%$ had private health insurance (Table 1). In contrast, $< 45\%$ of youth with type 2 diabetes were from families with annual family income of $\geq \$50,000$ and 62% had private health insurance.

Clinical characteristics

Table 1 presents clinical characteristics according to age within diabetes type. Focusing first on NHW youth with type 1 diabetes, after adjustment for duration of diabetes, fasting C-peptide was lowest among youth aged 0–4 years (0.1 ng/ml), in whom having DKA at diagnosis was most common (28.9%). Adjusted prevalence of GAD65 positivity was most common among youth aged ≥ 15 years. Prevalence of having A1C $\geq 9.5\%$ was most common among youth aged ≥ 15

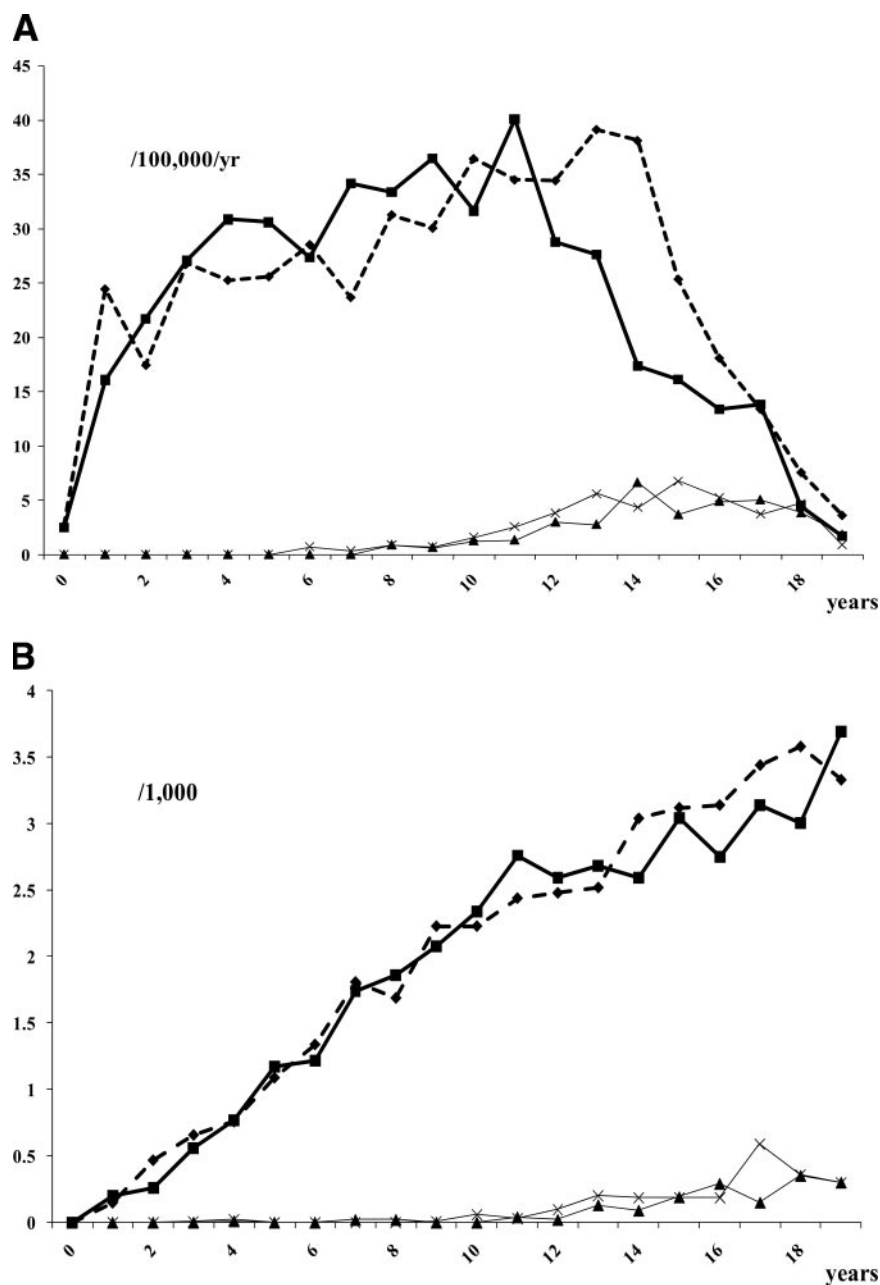


Figure 1—Incidence (A) and prevalence (B) of diabetes among NHW youth according to age, sex, and diabetes type. ◆, type 1 diabetic male subjects; ■, type 1 diabetic female subjects; ▲, type 2 diabetic male subjects; ×, type 2 diabetic female subjects.

years (21.5%) compared with prevalence that ranged from 3.4 to 11.2% across the younger age-groups.

About 30% of NHW youth with type 1 diabetes were overweight or obese. After adjustment for diabetes duration, $\leq 5\%$ had high blood pressure, either by blood pressure measurement or self-report of a provider diagnosis, with the exception of youth aged 0–4 years with prevalence of 12.9%. However, $>20\%$ of youth aged ≥ 15 years had either high triglyceride concentration or low HDL cholesterol af-

ter adjustment, and $>40\%$ of youth in each age-group had high LDL cholesterol. Adjusted prevalence of high ACR ranged from 5.6% (aged 5–9 years) to 10.4% (aged ≥ 15 years). Prevalence of high apoB was highest in the youngest and oldest age-groups.

For NHW youth with type 2 diabetes, clinical characteristics specific to diabetes did not differ significantly between younger (aged 10–14 years) and older youth (aged ≥ 15 years). However, as expected, fasting C-peptide was substan-

tially higher (>3.0 ng/ml) and prevalence of GAD positivity was substantially lower ($<25\%$) among youth with type 2 compared with type 1 diabetes. Also as expected, the prevalence of DKA at onset was significantly lower among youth with type 2 diabetes ($<10\%$), for whom family history of diabetes was more common and for whom use of insulin was less common, compared with youth with type 1 diabetes ($P < 0.001$ for all). Forty-five percent of youth with type 2 diabetes used insulin, either alone (21.3%) or in combination with metformin (24.1%). There was a significant association between glycemic control and diabetes type, with a higher proportion of youth with type 2 diabetes having good glycemic control (76.4%) compared with youth with type 1 diabetes (52.4%) ($P < 0.0001$).

NHW youth with type 2 diabetes had substantially higher prevalence of being overweight or obese compared with youth with type 1 diabetes ($P < 0.0001$). Moreover, the prevalence of having high blood pressure, high triglycerides, and low HDL cholesterol was higher among youth with type 2 diabetes compared with youth with type 1 diabetes ($P < 0.0001$ for all). Median apoB values were significantly higher for type 2 compared with type 1 diabetic youth. Over 40% of youth with type 2 diabetes had high LDL cholesterol, which was similar to the prevalence of high LDL cholesterol among youth with type 1 diabetes. The prevalence of high ACR was also higher among youth with type 2 compared with those with type 1 diabetes.

Behavioral characteristics

Behavioral characteristics can be found in Table 2. Current smoking was more common among NHW youth with type 2 compared with youth with type 1 diabetes (19.8 vs. 8.8%, $P < 0.0001$). Participation in moderate- or vigorous-intensity physical activity ≥ 3 days/week was reported by at least 49% of each age- and diabetes-type group but was less common among youth with type 2 compared with type 1 diabetes ($P = 0.03$). Across all age- and diabetes-type groups, percent of energy from saturated fat was nearly twice the recommendation of $<7\%$ (24).

CONCLUSIONS— With a population of >2 million youth under surveillance for prevalence and >20 million person-years for which diabetes incidence is estimated, the SEARCH study

Table 1—Sociodemographic and clinical characteristics of youth with type 1 or type 2 diabetes: the SEARCH study prevalent 2001 and incident 2002–2005 cases

| | Type 1 diabetes | | | | P* | Type 2 diabetes | | | P† | P‡ |
|--|-----------------|------------|--------------|------------|---------|-----------------|------------|--------|---------|---------|
| | 0–4 | 5–9 | 10–14 | ≥15 | | 10–14 | ≥15 | P‡ | | |
| Sociodemographic characteristics | | | | | | | | | | |
| Income | | | | | 0.0036 | | | | 0.9565 | <0.0001 |
| <\$25,000 | 27 (9.8) | 80 (9.9) | 116 (9.6) | 73 (8.6) | | 11 (29.7) | 20 (31.7) | | | |
| \$25,000–\$49,000 | 78 (28.4) | 183 (22.6) | 223 (18.5) | 168 (19.8) | | 9 (24.3) | 17 (27) | | | |
| \$50,000–\$74,000 | 71 (25.8) | 169 (20.9) | 287 (23.8) | 190 (22.4) | | 10 (27) | 14 (22.2) | | | |
| ≥\$75,000 | 99 (36) | 376 (46.5) | 580 (48.1) | 417 (49.2) | | 7 (18.9) | 12 (19) | | | |
| Education | | | | | 0.0190 | | | | 0.7478 | 0.0003 |
| Less than high school | 1 (0.3) | 12 (1.4) | 31 (2.5) | 11 (1.2) | | 3 (7.1) | 4 (5.6) | | | |
| High school graduate or higher | 295 (99.7) | 832 (98.6) | 1231 (97.5) | 940 (98.8) | | 39 (92.9) | 67 (94.4) | | | |
| Insurance§ | | | | | <0.0001 | | | | 0.0466 | <0.0001 |
| Private | 220 (78.6) | 637 (81.5) | 981 (84.6) | 744 (87) | | 30 (78.9) | 33 (52.4) | | | |
| Medicaid/Medicare | 54 (19.3) | 127 (16.2) | 150 (12.9) | 78 (9.1) | | 8 (21.1) | 26 (41.3) | | | |
| Other | 3 (1.1) | 13 (1.7) | 13 (1.1) | 15 (1.8) | | | 2 (3.2) | | | |
| None | 3 (1.1) | 5 (0.6) | 15 (1.3) | 18 (2.1) | | | 2 (3.2) | | | |
| Clinical characteristics | | | | | | | | | | |
| Fasting C-peptide (adjusted means ± SE) | 0.1 ± 0.04 | 0.3 ± 0.02 | 0.5 ± 0.02 | 0.6 ± 0.02 | <0.0001 | 3.4 ± 0.4 | 3.7 ± 0.3 | 0.5892 | <0.0001 | |
| GAD antibody positive | 115 (55) | 371 (51.5) | 618 (54.4) | 451 (51) | 0.3690 | 6 (15) | 15 (23.4) | 0.2970 | <0.0001 | |
| Duration adjusted (%) | 46.4 | 46.3 | 52.9 | 59 | <0.0001 | 14.8 | 23.6 | 0.2981 | <0.0001 | |
| DKA at onset [n (% yes)] | 73 (28.9) | 94 (18.5) | 143 (24) | 37 (15.8) | 0.0007 | 3 (8.8) | 1 (2.6) | 0.2411 | 0.0008 | |
| Family history of diabetes | | | | | <0.0001 | | | | 0.9734 | <0.0001 |
| Yes¶ | 133 (44.8) | 404 (47.9) | 714 (56.8) | 528 (55.1) | | 32 (78) | 56 (77.8) | | | |
| No | 164 (55.2) | 439 (52.1) | 544 (43.2) | 430 (44.9) | | 9 (22) | 16 (22.2) | | | |
| Diabetes therapy (current) | | | | | 0.0020 | | | | 0.7264 | <0.0001 |
| Insulin | 297 (100) | 835 (99.4) | 1,245 (98.7) | 927 (97.1) | | 10 (25) | 13 (19.1) | | | |
| Metformin | | | 3 (0.2) | 2 (0.2) | | 19 (47.5) | 34 (50) | | | |
| Both | | 5 (0.6) | 12 (1) | 23 (2.4) | | 8 (20) | 18 (26.5) | | | |
| None | | | 1 (0.1) | 3 (0.3) | | 3 (7.5) | 3 (4.4) | | | |
| A1C | | | | | <0.0001 | | | | 0.3267 | <0.0001 |
| < 8% | 108 (52.7) | 433 (59.7) | 622 (53.6) | 399 (44.7) | | 29 (70.7) | 52 (80) | | | |
| 8–9.5% | 90 (43.9) | 255 (35.2) | 408 (35.2) | 302 (33.8) | | 7 (17.1) | 5 (7.7) | | | |
| ≥9.5% | 7 (3.4) | 37 (5.1) | 130 (11.2) | 192 (21.5) | | 5 (12.2) | 8 (12.3) | | | |
| BMI z score | 0.6 ± 1 | 0.6 ± 0.9 | 0.6 ± 0.9 | 0.6 ± 0.9 | 0.9554 | 1.9 ± 0.8 | 2.1 ± 0.6 | 0.1331 | <0.0001 | |
| Weight | | | | | 0.4615 | | | | 0.0773 | <0.0001 |
| Underweight/normal | 127 (70.2) | 575 (69.8) | 840 (68.2) | 641 (69.1) | | 7 (17.1) | 3 (4.7) | | | |
| Overweight 85th–95th percentile | 37 (20.4) | 148 (18) | 260 (21.1) | 194 (20.9) | | 3 (7.3) | 9 (14.1) | | | |
| Obese ≥95th percentile | 17 (9.4) | 101 (12.3) | 131 (10.6) | 92 (9.9) | | 31 (75.6) | 52 (81.3) | | | |
| High waist circumference** | 36 (20.8) | 97 (11.9) | 162 (13.4) | 125 (14) | 0.0214 | 33 (78.6) | 55 (87.3) | 0.2342 | <0.0001 | |
| Acanthosis nigricans [n (% yes)] | 3 (1.6) | 9 (1.1) | 26 (2.1) | 18 (2) | 0.3499 | 16 (43.2) | 16 (25.8) | 0.0727 | <0.0001 | |
| High blood pressure†† | 22 (13.1) | 41 (5.1) | 53 (4.4) | 39 (4.2) | <0.0001 | 13 (31.7) | 4 (6.2) | 0.0005 | <0.0001 | |
| Duration adjusted (%) | 12.9 | 5 | 4.4 | 4.3 | 0.0001 | 30.6 | 6.3 | 0.0033 | <0.0001 | |
| Self-reported hypertension | | 6 (0.7) | 16 (1.3) | 62 (6.5) | <0.0001 | 11 (26.8) | 22 (31.4) | 0.6089 | <0.0001 | |
| Duration adjusted (%) | | 0.8 | 1.3 | 5 | <0.0001 | 26.2 | 31.8 | 0.5463 | <0.0001 | |
| High triglycerides (≥110 mg/dl) | 3 (1.8) | 26 (4) | 115 (10.8) | 204 (25) | <0.0001 | 21 (56.8) | 39 (60.9) | 0.6802 | <0.0001 | |
| Duration adjusted (%) | 2.1 | 4.4 | 11 | 22.1 | <0.0001 | 57.9 | 60.4 | 0.8147 | <0.0001 | |
| Low HDL cholesterol (≤40 mg/dl) | 27 (13.4) | 45 (6.3) | 123 (10.7) | 163 (18.3) | <0.0001 | 21 (52.5) | 46 (69.7) | 0.0751 | <0.0001 | |
| Duration adjusted (%) | 11.8 | 5.8 | 10.3 | 20.1 | <0.0001 | 46.7 | 74.1 | 0.0113 | <0.0001 | |
| High LDL cholesterol (≥100 mg/dl) | 91 (53.8) | 291 (45.3) | 445 (41.9) | 369 (45.2) | 0.0275 | 16 (43.2) | 36 (56.3) | 0.2076 | 0.1654 | |
| Duration adjusted (%) | 57.9 | 47.8 | 42.7 | 41.3 | 0.0006 | 44.5 | 55.5 | 0.3049 | 0.0631 | |
| ApoB [median (interquartile range)] | 75 (17.5) | 71 (22) | 71 (23) | 76 (26) | <0.0001 | 83 (32) | 90 (40) | 0.1049 | <0.0001 | |
| Duration adjusted [median (interquartile range)] | 74.8 (0.7) | 68.3 (2.0) | 70.1 (3.2) | 76.4 (5.3) | <0.0001 | 79.6 (2.3) | 89.7 (7.1) | 0.2220 | <0.0001 | |
| High ACR (≥30) | 13 (6.9) | 40 (5.4) | 112 (10.1) | 89 (10.8) | 0.0006 | 5 (11.9) | 9 (15.3) | 0.6311 | 0.0872 | |
| Duration adjusted (%) | 7.1 | 5.6 | 10.2 | 10.4 | 0.0036 | 13.3 | 12.7 | 0.9342 | 0.0498 | |

Data are n (%), unless otherwise indicated. Physical examination data not collected on youth aged <3 years. *For categorical variables using χ^2 test for the association between variable levels and age-groups within type 1 diabetes; for continuous variables using ANOVA for the overall effect of age-group within type 1 diabetes; for adjusted variables using logistic regression (categorical variables) or linear regression (continuous variables) for the overall effect of age-group within type 1 diabetes. †For categorical variables using χ^2 test for the association between variable levels and age-groups within type 2 diabetes; for continuous variables using ANOVA for the overall effect of age-group within type 2 diabetes; for adjusted variables using logistic regression (categorical variables) or linear regression (continuous variables) for the overall effect of age-group within type 2 diabetes. ‡For categorical variables using χ^2 test for the association between variable levels and diabetes type (type 1 versus type 2); for continuous variables using ANOVA for the overall effect of diabetes type (type 1 versus type 2); for adjusted variables using logistic regression (categorical variables) or linear regression (continuous variables) for the overall effect of diabetes type (type 1 versus type 2). §Only nonmembership sites (South Carolina, Ohio, Washington, and Colorado). ||Incident cases only. ¶Family history includes parents, grandparents, and biological siblings. **Waist circumference ≥90th percentile for age and sex. ††Measured blood pressure (systolic or diastolic) ≥ age-, sex-, and height-specific 95th percentile.

Table 2—Behavioral characteristics of youth with type 1 or type 2 diabetes: the SEARCH study prevalent 2001 and incident 2002–2005 case subjects aged ≥ 10 years

| | Type 1 diabetes | | | Type 2 diabetes | | | P [‡] | P [‡] |
|---------------------------------|-----------------|----------------|---------|-----------------|----------------|----------------|----------------|----------------|
| | 10–14 | ≥ 15 | P* | 10–14 | ≥ 15 | P [†] | | |
| Smoking | | | <0.0001 | | | 0.0079 | <0.0001 | |
| Never | 1,143 (93.5) | 531 (57.2) | | 32 (78) | 31 (47.7) | | | |
| Former | 60 (4.9) | 227 (24.5) | | 5 (12.2) | 17 (26.2) | | | |
| Current | 19 (1.6) | 170 (18.3) | | 4 (9.8) | 17 (26.2) | | | |
| Physically active | | | 0.0003 | | | 0.6570 | 0.0300 | |
| 0–2 days/week | 431 (35.2) | 398 (42.8) | | 19 (46.3) | 33 (50.8) | | | |
| 3–7 days/week | 792 (64.8) | 531 (57.2) | | 22 (53.7) | 32 (49.2) | | | |
| % Kcal from fat | | | | | | | | |
| Total fat | 37.8 \pm 5.9 | 38.3 \pm 5.9 | 0.0433 | 39.1 \pm 7.5 | 39.8 \pm 5.4 | 0.6169 | 0.0194 | |
| Saturated fat | 13.7 \pm 2.3 | 13.8 \pm 2.4 | 0.3309 | 13.8 \pm 2.6 | 14.5 \pm 2.2 | 0.2219 | 0.0809 | |
| Fruits, vegetables servings/day | 2.7 \pm 1.8 | 3.1 \pm 2.1 | <0.0001 | 3.2 \pm 3 | 2.5 \pm 1.6 | 0.1665 | 0.7192 | |
| High CES-D score (≥ 24) | 65 (5.3) | 66 (7.1) | 0.0852 | 9 (22) | 11 (17.5) | 0.5701 | <0.0001 | |

Data are n (%) or means \pm SD. *For categorical variables using χ^2 test for the association between variable levels and age-groups within type 1 diabetes; for continuous variables using ANOVA for the overall effect of age-group within type 1 diabetes; for adjusted variables using logistic regression (categorical variables) or linear regression (continuous variables) for the overall effect of age-group within type 1 diabetes. †For categorical variables using χ^2 test for the association between variable levels and age-groups within type 2 diabetes; for continuous variables using ANOVA for the overall effect of age-group within type 2 diabetes; for adjusted variables using logistic regression (categorical variables) or linear regression (continuous variables) for the overall effect of age-group within type 2 diabetes. ‡For categorical variables using χ^2 test for the association between variable levels and diabetes type (type 1 versus type 2); for continuous variables using ANOVA for the overall effect of diabetes type (type 1 versus type 2); for adjusted variables using logistic regression (categorical variables) or linear regression (continuous variables) for the overall effect of diabetes type (type 1 versus type 2). CES-D, Centers for Epidemiologic Study Depression Scale.

represents the largest standardized registry of diabetes in NHW youth in the U.S.

We found an overall prevalence of type 1 diabetes of 2.0/1,000 in NHW youth aged <20 years. In general, the prevalence of type 1 diabetes in children aged <15 years ranges from 0.5/1,000 to 3/1,000 in most European and North American populations (25). Comparisons of prevalence estimates across populations may be subject to bias, since prevalence is determined not only by disease incidence but also by migration and survival, which may vary markedly by country or region. Prevalence data, however, are useful in determining the public health impact of a specific condition. Based on the SEARCH study data, we estimated that in 2001, the number of type 1 diabetic NHW youth aged <20 years in the U.S. was \sim 100,300 (2).

To facilitate comparison with published data from prior registries in Europe and the U.S., we also estimated the age-standardized annual incidence of type 1 diabetes in NHW SEARCH study youth aged 0–14 years (Table 3). The age-standardized annual incidence of type 1 diabetes among NHW SEARCH study youth aged 0–14 years was 27.5/100,000. European studies, which typically show the highest rates of type 1 diabetes of any population in the world, also show large rate variations across geographic areas. Rates of type 1 diabetes re-

ported by the DiaMond study throughout the 1990s among youths aged 0–14 years in European countries ranged from 5.3/100,000 in Bucharest, Romania, and 7.6/100,000 in Cracow, Poland, to 20/100,000

in Norway, and >40/100,000 in Finland (4,26) (Table 3). Therefore, the incidence of type 1 diabetes among NHW children aged 0–14 years reported by the SEARCH study is one of the highest in the world.

Table 3—Age-standardized incidence of type 1 diabetes in Caucasian children aged ≤ 14 years (per 100,000/year) from selected studies

| Region (country and area) | Study period | Incidence | | |
|--|--------------|---------------|-----------------|--------------------|
| | | Male subjects | Female subjects | Total (95% CI) |
| Selected European countries* | | | | |
| Finland | 1990–1999 | 41.9 | 39.9 | 40.9 (39.6–42.2) |
| Italy (Sardinia) | 1990–1998 | 45.0 | 30.6 | 37.8 (35.5–40.3) |
| Sweden | 1990–1999 | 30.5 | 29.4 | 30.0 (29.1–30.8) |
| Norway (eight counties) | 1990–1999 | 21.6 | 19.9 | 20.8 (19.4–22.1) |
| U.K. (Plymouth) | 1990–1999 | 17.1 | 20.8 | 19.0 (16.8–21.2) |
| Germany (Baden-Württemberg) | 1990–1998 | 12.7 | 12.6 | 12.6 (12.1–13.2) |
| Slovakia | 1990–1999 | 9.7 | 9.7 | 9.7 (9.2–10.3) |
| Italy (Lazio) | 1990–1999 | 8.9 | 8.6 | 8.8 (8.1–9.4) |
| Lithuania | 1990–1999 | 7.6 | 8.2 | 7.9 (7.3–8.5) |
| Poland (Cracow) | 1990–1999 | 7.5 | 7.6 | 7.6 (7.0–8.2) |
| Romania (Bucharest) | 1990–1999 | 4.7 | 5.9 | 5.3 (4.7–6.1) |
| Selected U.S. studies in Caucasian populations | | | | |
| U.S. (SEARCH) | 2002–2005 | 27.9 | 27.0 | 27.5 (26.4, 28.6) |
| U.S. (Allegheny)* | 1990–1994 | 19.1 | 16.4 | 17.8 (15.45–20.33) |
| U.S. (Philadelphia)† | 1995–1999 | | | 13.0 (10.2–15.6) |
| U.S. (Chicago)* | 1995–1999 | 19.0 | 17.5 | 18.3 (15.7–22.2) |
| U.S. (Alabama)* | 1990–1995 | 14.1 | 15.1 | 14.6 (12.2–18.2) |
| U.S. (Colorado)‡ | 1978–1988 | 17.5 | 15.5 | 16.4 (15.0–17.8) |

*Based on ref. 26. †Based on ref. 30. ‡Based on ref. 27.

Additionally, SEARCH study type 1 diabetes incidence rates for youth aged <15 years were 68% higher than those reported in the 1980s in Colorado (27); 88 and 54% higher than those reported in the early 1990s in Alabama and Allegheny county, respectively (28,29); and 111 and 50% higher than noted in the late 1990s in Philadelphia (30) and Chicago, respectively (31). These data suggest that the incidence of type 1 diabetes in NHW youth may be increasing in the U.S., which would be consistent with worldwide trends (32).

There is a paucity of data on type 2 diabetes among NHW youth. In the SEARCH study, type 2 diabetes was exceptionally rare among NHW youth aged <10 years. Even among youth aged 10–19 years, the annual incidence rate was only 3.7/100,000. Similarly, data from the Chicago registry indicated rates of non-type 1 diabetes among youth aged 0–17 years of 2.8/100,000 in 2003 (31). However, recent studies (33,34) from Europe show prevalence and incidence estimates much lower than those reported in the present study, indicating that type 2 diabetes remains a rarity in these populations. For example, studies from Germany, Austria, France, and the U.K. (35–37) all show type 2 diabetes accounting for only 1–2% of all pediatric diabetes cases. Using an Austrian national register, Rami et al. (38) found that type 2 diabetes represented only 1.5% of all newly diagnosed cases of diabetes in those aged <15 years from 1999–2001, giving an incidence of 0.025/100,000 per year. A single center in France (36) reported that only 2% of 382 children (aged 1–16 years) with diabetes had type 2 diabetes. In contrast, in the SEARCH study, type 2 diabetes accounted for almost 15% of all diabetes cases among NHW adolescents aged ≥ 10 years (3). A survey of all children (aged 0–16 years) with diabetes from 177 British pediatric diabetes centers found a prevalence of type 2 diabetes of 0.002/1,000 (39). In contrast, SEARCH study data show a prevalence of diagnosed type 2 diabetes among those aged 10–19 years that is ~ 100 -fold higher than the British estimates (0.18/1,000). Differences in physical activity levels or food choices and subsequent obesity rates between populations may partly explain the lower type 2 diabetes prevalence and incidence in European studies compared with SEARCH study data; however, the full explanation for these discrepancies remains unclear.

The age distribution of incidence rates of type 1 diabetes in this population is consistent with very recent data from Finland (40) and different from that noted among Colorado non-Hispanic youth in the 1980s (25), suggesting that age at onset of type 1 diabetes has been decreasing over time. Interestingly, the incidence rates of type 1 diabetes seem to peak at an earlier age for female compared with male subjects, again consistent with recent data from Finland, the country with the highest incidence of type 1 diabetes in the world (40). Consistent with numerous previous studies (41–43), the peak age at onset of type 2 diabetes in our population is around puberty (aged 14–15 years), a period thought to coincide with a physiological rise in insulin resistance.

There was a fairly consistent pattern of incidence of diabetes for NHW youth compared with other racial and ethnic groups in the SEARCH study (3). For all age-groups, incidence rates of type 1 diabetes were highest for NHW youth compared with the other racial and ethnic groups (African American, Hispanic, Asian/Pacific Islander, and Navajo; online appendix tables). Conversely, rates for type 2 diabetes were consistently lowest across age-groups for NHW youth compared with the other four groups. Incidence rates for type 2 diabetes among African American youth were more than fourfold higher and among Navajo youth about sevenfold higher compared with NHW youth. Further investigation is needed to more fully understand these patterns.

The SEARCH study conducted a comprehensive examination of sociodemographic, clinical, and behavioral characteristics of youth with diabetes. In adult populations, type 2 diabetes has been associated with lower socioeconomic status (44), consistent with markers of lower socioeconomic status observed in the present study among youth with type 2 compared with type 1 diabetes. Also consistent with this finding, Eppens et al. (45) reported a comparison of 1,433 Australian adolescents with type 1 diabetes and 68 similarly aged youth with type 2 diabetes and found worse social disadvantage score among those with type 2 diabetes ($P = 0.058$).

Scott et al. (42) compared clinical characteristics between youth with type 1 and type 2 diabetes at the time of diagnosis and found similar A1C but substantially higher C-peptide level and higher

prevalence of obesity among those with type 2 diabetes. From the work of Eppens et al. (45), with average diabetes duration of 6.8 years for youth with type 1 diabetes and 1.3 years for those with type 2 diabetes, A1C was significantly lower among those with type 2 compared with those with type 1 diabetes, similar to the present results.

A significant excess prevalence of components of the metabolic syndrome, and of the metabolic syndrome itself using the age-modified definition of the National Cholesterol Education Program Adult Treatment Panel III criteria, was previously reported by the SEARCH study for youth with type 2 compared with those with type 1 diabetes (46). That study showed that NHW youth had the lowest prevalence of metabolic syndrome compared with the racial and ethnic groups represented in the SEARCH study. This study also showed that NHW youth had the lowest prevalence of high blood pressure, low HDL cholesterol, and high waist circumference.

Eppens et al. (45) similarly reported higher prevalence of hypertension, obesity, and microalbuminuria among youth with type 2 compared with those with type 1 diabetes. Wadwa (47) recently reviewed cardiovascular disease (CVD) risk in youth with diabetes, with an emphasis on type 1 diabetes because of its greater prevalence among youth compared with type 2 diabetes. As noted by Wadwa (47), it is important to emphasize the high prevalence of CVD risk factors in youth with type 2 diabetes and, at the same time, to take note that by age 55 years an estimated 35% of individuals with type 1 diabetes die of coronary artery disease compared with 8% of nondiabetic men and 4% of nondiabetic women.

In the present study, among youth with type 1 diabetes aged ≥ 15 years, >20% had high triglyceride or low HDL cholesterol concentrations, and >40% had LDL cholesterol ≥ 100 mg/dl after adjusting for diabetes duration. Schwab et al. (48) reported analyses from records from a large cohort of youth with type 1 diabetes registered across 195 medical centers and found prevalence of CVD risk factors including dyslipidemia, hypertension, BMI z score, and smoking to be more common among older (aged 17–26 years) compared with younger subjects (aged <17 years). The prevalence of dyslipidemia was 34% among older individuals, and elevated systolic blood pressure was 11%. Unique in this analysis is the

reporting of levels of apoB in youth with type 1 and type 2 diabetes, which was particularly high among older youth with type 2 diabetes. A recent consensus report from the American Diabetes Association and the American College of Cardiology (49) suggests treatment guidelines for apoB of <90 mg/dl (the median for older youth with type 2 in the SEARCH study) for high-risk diabetic patients (no other CVD risk factors) and <80 mg/dl for highest-risk patients (one or more additional CVD risk factors). In a previous SEARCH study report, Albers et al. (50) reported high rates of elevated apoB and dense LDL cholesterol among youth with type 2 diabetes, particularly those with poor glycemic control. Further research is needed to more fully understand these CVD risk factors in youth with diabetes.

In multivariate analyses, overweight was most closely associated with number of CVD risk factors, followed by age. About 30% of youth with type 1 diabetes in the SEARCH study were overweight or obese, and lifestyle behaviors potentially conducive to difficulties in weight management including high prevalence of physical inactivity and low intake of fruits and vegetables were common. Thus, future studies should focus on the problem of overweight and obesity among youth not only with type 2 diabetes but also among youth with type 1 diabetes, with consideration of both the metabolic impact of overweight and obesity for youth with diabetes and healthy approaches to weight management.

This report has some limitations that must be considered. First, analyses derive from the initial research visit only and thus are cross-sectional, so we are unable to examine factors such as the clinical course of diabetes in these participants. Prospective data collection is underway. Furthermore, a substantial proportion of youth did not participate in the research visit. Across all racial/ethnic groups in the SEARCH study, participation in this visit was lower for older youth, youth with type 2 versus type 1 diabetes, and among African Americans (51). For this analysis, ~52% of all registered NHW patients had a research visit. However, we did show previously that using a weighted estimate based on age, sex, race/ethnicity, diabetes type, and diabetes duration distribution for all registered case subjects did not substantially change our findings in estimating the prevalence of elevated albumin (52).

Nonetheless, the SEARCH study is one of the largest, most comprehensive

studies of diabetes in NHW youth. This analysis provided a unique opportunity to examine the burden of diabetes among NHW youth in the U.S. According to the SEARCH study, the incidence of type 1 diabetes in NHW youth in the U.S. is now one of the highest in the world, with rates similar to those reported by northern European countries. Type 2 diabetes is still a relatively rare condition among NHW U.S. adolescents, but rates are several-fold higher than those reported by several European countries. Further research from the SEARCH study will allow for the estimation of trends in incidence of diabetes among NHW youth, according to diabetes type and sex. Additionally, efforts directed at improving the cardiometabolic and behavioral risk factor profile in this population are warranted.

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