The SEARCH for Diabetes in Youth Study: Rationale, Findings, and Future Directions

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REVIEW

The SEARCH for Diabetes in Youth (SEARCH) study was initiated in 2000, with funding from the Centers for Disease Control and Prevention and support from the National Institute of Diabetes and Digestive and Kidney Diseases, to address major knowledge gaps in the understanding of childhood diabetes. SEARCH is being conducted at five sites across the U.S. and represents the largest, most diverse study of diabetes among U.S. youth. An active registry of youth diagnosed with diabetes at age <20 years allows the assessment of prevalence (in 2001 and 2009), annual incidence (since 2002), and trends by age, race/ethnicity, sex, and diabetes type. Prevalence increased significantly from 2001 to 2009 for both type 1 and type 2 diabetes in most age, sex, and race/ethnic groups. SEARCH has also established a longitudinal cohort to assess the natural history and risk factors for acute and chronic diabetes-related complications as well as the quality of care and quality of life of persons with diabetes from diagnosis into young adulthood. Many youth with diabetes, particularly those from low-resourced racial/ethnic minority populations, are not meeting recommended guidelines for diabetes care. Markers of micro- and macrovascular complications are evident in youth with either diabetes type, highlighting the seriousness of diabetes in this contemporary cohort. This review summarizes the study methods, describes key registry and cohort findings and their clinical and public health implications, and discusses future directions.

Significant gaps existed at the start of the 21st century in our understanding of diabetes in youth, including limited data on the burden of diabetes and trends in incidence and prevalence by type, age, sex, and race/ethnicity, the natural history and etiologic classification of childhood diabetes, the burden and risk factors for diabetes-related early complications, and the quality of health care and quality of life of youth with diabetes. The SEARCH for Diabetes in Youth (SEARCH) study was initiated in 2000 with funding from the Division of Diabetes Translation of the Centers for Disease Control and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases of the National Institutes of Health to address these gaps and respond to emerging issues in the field of childhood diabetes. SEARCH has brought together multiple facets of childhood diabetes research: an active epidemiologic surveillance component to assess trends in incidence, prevalence, and clinical course and a health services research component to evaluate the processes and quality of care using both clinical and public health perspectives. We provide a description of the methods used and an overview of major findings to date as well as future questions and challenges to be addressed to develop a more complete picture of diabetes in youth.

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DESIGN OF SEARCH

Recruitment

Phase 1 (2000–2005) (1) and 2 (2005–2010) included six recruitment centers, four geographic-based sites based in Ohio (eight counties including Cincinnati, OH); the entire state of Colorado; five counties around Seattle, Washington; the entire state of South Carolina; two health plan–based sites in Hawaii and California (health plan enrollees in one plan from seven counties); and under the direction of Colorado, American Indian reservation-based populations in Arizona and New Mexico. Each site identified prevalent (in 2001 and 2009) and incident cases (ongoing since 2002) of diagnosed diabetes (excluding gestational diabetes) in youth <20 years of age. Phase 3 began in 2010 and continues to the present with five of the six original centers (excluding Hawaii).

Study Components

SEARCH includes a registry and a cohort study (Fig. 1). The registry study identifies incident cases each year since 2002 through the present with ~5.5 million children <20 years of age (~6% of the U.S. population <20 years) under surveillance annually. Approximately 3.5 million children <20 years of age were under surveillance in 2001 at the six SEARCH recruitment centers, with approximately the same number at the five centers under surveillance in 2009. Denominators representing the population at risk for the geographic-based sites use race-bridged postcensal estimates of the nonmilitary, noninstitutionalized midyear populations in the center catchment areas. The health plans use end-of-year membership rolls, and Indian Health Service beneficiary rolls provide American Indian site denominators. Compared with U.S. Census data, the SEARCH surveillance population is similar to the U.S. youth population with respect to race/ethnicity, age, household income, and parental education (2).

Centers conduct active surveillance under Health Insurance Portability and Accountability Act waivers of consent using networks of endocrinologists (pediatric and adult), as well other health care providers, hospitals, community health centers, clinical and administrative data systems, and electronic medical records. Cases are determined to be valid (diabetes is confirmed in the medical record or by the referring physician), eligible (based on age, residence, nonmilitary, noninstitutionalized, and health plan membership at diagnosis [health plan sites]), and unique (duplicates are removed) locally and are then registered anonymously with the Coordinating Center at Wake Forest University. A high degree of case ascertainment (generally >90%), for both type 1 and type 2 diabetes has been obtained, estimated using capture-recapture methods (2–4).

The cohort study was developed by recruiting incident cases in 2002–2006, 2008, and 2012 that had a baseline visit near diagnosis and at least 5 years of diabetes duration at the cohort visit assessment (Fig. 1). The cohort study will allow estimates of the prevalence and incidence of acute and chronic complications as well as the degree to which processes of care impact glycemia, blood pressure, and lipid control and diabetes-related outcomes. A biospecimen repository has also been developed and is available for the conduct of ancillary studies.

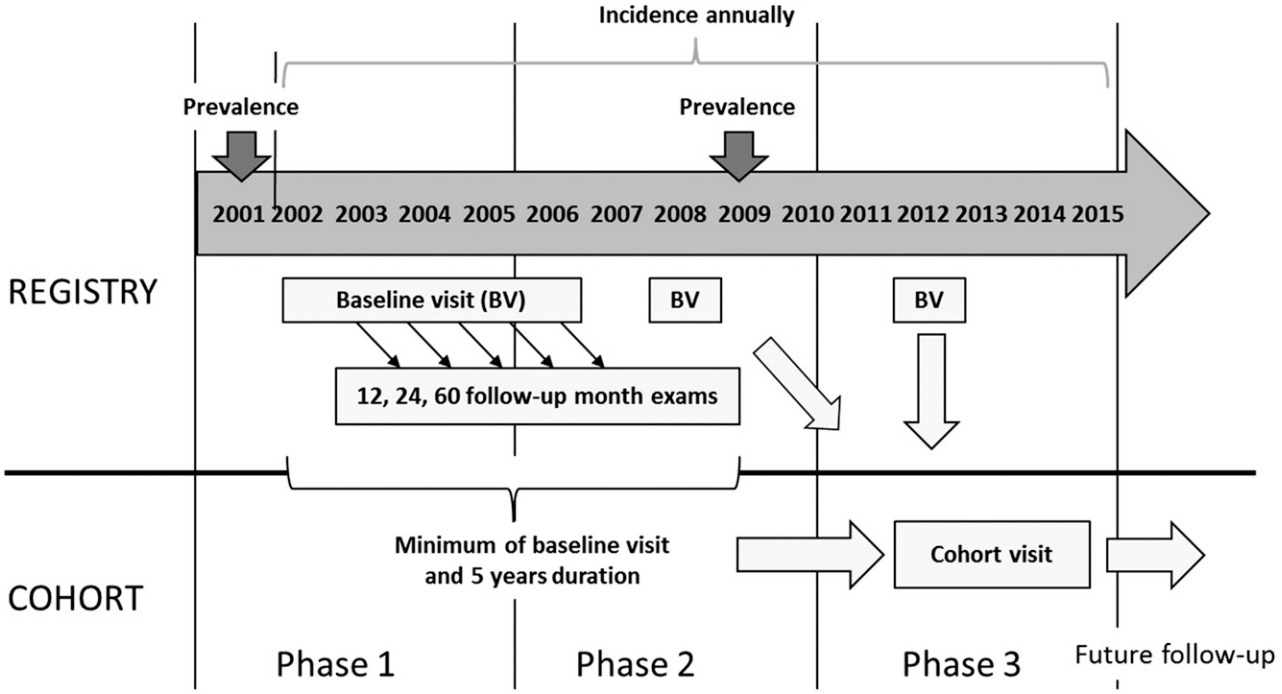

Figure 1—Summary of the SEARCH study design. The registry began in 2001 measuring prevalence, which was repeated in 2009. Incidence has been measured annually starting in 2002. Youth diagnosed in 2002–2006, 2008, and 2012 had a baseline in-person visit for measurement of diabetes autoantibodies, albuminuria, BMI, cardiovascular risk factors, and sociodemographic, quality of care, and quality of life questionnaires. Youth with baseline visits (incident cases in 2002–2005) were invited to return in 12, 24, and 60 months after their baseline visit for additional visits. Those with a baseline visit and at least 5 years of duration were asked to join the cohort study, started in 2012, which added measures of early complications (retinopathy, cardiac autonomic and peripheral neuropathy, and arterial stiffness). Future follow-up of the cohort is planned.

STUDY FINDINGS

Diabetes Is Frequent Among U.S. Youth, and Both Type 1 and Type 2 Diabetes Are Increasing in Most Racial/Ethnic Populations and Sex and Age Groups

The prevalence of all types of diabetes was 1.8/1,000 youth in 2001 and was 2.2/1,000 youth in 2009, which translated to at least 154,000 children/youth in the U.S. with diabetes in 2001 (5) and at least 192,000 in 2009 (6). Overall, between 2001 and 2009, prevalence of type 1 diabetes in youth increased by 21.1% (95% CI 15.6–27.0), with similar increases for boys and girls and in most racial/ethnic and age groups (2) (Fig. 2). The prevalence of type 2 diabetes also increased significantly over the same time period by 30.5% (95% CI 17.3–45.1), with increases observed in both sexes, 10–14- and 15–19-year-olds, and among Hispanic and non-Hispanic white and African American youth (2). These data on changes in type 2 are consistent with smaller U.S. studies (7–11).

The incidence of diabetes (per 100,000/year) in 2002 to 2003 was 24.6/100,000/year (12), representing ~15,000 new patients every year with type 1 diabetes and 3,700 with type 2 diabetes, increasing to 18,436 newly diagnosed type 1 and 5,089 with type 2 diabetes in 2008 to 2009 (13). Among non-Hispanic white youth, the incidence of type 1 diabetes increased by 2.7% (95% CI 1.2–4.3) annually between 2002 and 2009. Significant increases were observed among all age groups except the youngest age group (0–4 years) (14). These increases for non-Hispanic whites are consistent with data worldwide (15,16), with the highest increase in the 0–4-year age group (5.4% per year) (17), something not seen in SEARCH results. The underlying factors responsible for this increase have not yet been identified. Potential trends in incidence of type 1 and type 2 diabetes among other racial/ethnic groups are currently being explored.

Diabetes presents a significant burden to the health of U.S. youth and represents a major clinical and public health challenge, especially with increasing burden of both types of diabetes in minority youth and unique challenges in proper diagnosis and management (18), given excess obesity in minorities.

Many Youth With Diabetes, Particularly Those of Racial and Ethnic Minority Groups, Are at Risk for Acute and Chronic Complications

Over 50% of youth are hospitalized at diabetes onset, and ~30% of children newly diagnosed with diabetes present with diabetic ketoacidosis (DKA) (19). Prevalence of DKA at diagnosis was three times higher among youth with type 1 diabetes (29.4%) compared with youth with type 2 diabetes (9.7%) and was lowest in Asian/Pacific Islanders (16.2%) and highest among Hispanics (27.0%).

A substantial proportion of youth with diabetes, particularly African American and American Indian youth and especially youth with type 2 diabetes, come from low-resourced homes (60–70%) (20–24). Overweight [85–94% of U.S. BMI distribution (25)] and obesity (≥95% of the U.S. BMI distribution) are common among youth with type 2 diabetes regardless of race/ethnicity (80–90%). However, a surprisingly large proportion of youth with type 1 diabetes (35–50%) were also overweight or obese across all racial/ethnic groups (20–24). This high rate of overweight/obesity is at least partly due to low rates of physical activity (26) and low consumption of fruits and vegetables (27).

A significant proportion of youth with diabetes, particularly those with type 2 diabetes, have very poor glycemic control (Table 1) (28): 17% of youth with type 1 diabetes and 27% of youth with type 2 diabetes had A1C levels ≥9.5% (≥80 mmol/mol). Minority youth were significantly more likely to have higher A1C levels compared with non-Hispanic white youth, regardless of diabetes type. Table 1 also shows that cardiovascular disease risk factors were also elevated, including high blood pressure and dyslipidemia (29–31), elevated apolipoprotein B (apoB) levels and small, dense LDL particles (32). Early signs of kidney disease (33), retinopathy (34), neuropathy (35,36), as well as increased arterial stiffness (37–39) were also identified. This was especially true for youth with type 2 diabetes and for racial and ethnic minority youth with type 1 diabetes. Youth with worse glycemic control had poorer levels of each of these outcomes. These data stress the need to enhance screening efforts for risk factors and preclinical disease in these

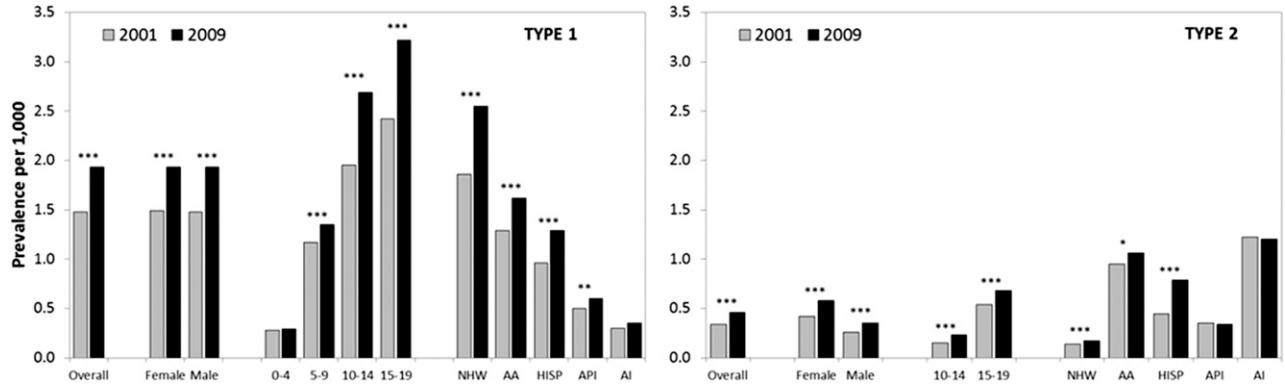

Figure 2—Prevalence (per 1,000) of diabetes by type, sex, age group, and race/ethnic group in 2001 and 2009 (2). *P* values for change between years: $*P < 0.05$; $**P < 0.01$; $***P < 0.001$. AA, African American; AI, American Indian; API, Asian Pacific Islander; HISP, Hispanic; NHW, non-Hispanic white.

Table 1—Prevalence of elevated glycemia, CVD risk factors, and early complications, SEARCH 2006–2013

	Type 1	*P* value	Type 2	*P* value
Glycemia (28)	*N* = 3,947		*N* = 552	
A1C ≥9.5% (≥80 mmol/mol), all races (%)	16.8		26.6	
Non-Hispanic white	12.3	<0.0001*	12.2	<0.0001*
African American	35.5		22.3	
Hispanic	27.3		27.4	
Asian Pacific Islander	26.0		36.4	
American Indian	52.2		43.8	
CVD risk factors†, age 10–19 years (30)	*N* = 1,376		*N* = 63	
Hypertension (%)	22.0		73.0	
Elevated triglycerides (%)	14.0		65.0	
Decreased HDL (%)	9.0		60.0	
Increased waist circumference (%)	15.0		95.0	
	N = 2,657		*N* = 345	
Elevated apoB (%) (32)	10.6		36.3	<0.0001‡
Dense LDL (%) (32)	7.9		36.3	
Retinopathy (34)	*N* = 222		*N* = 43	
Any (%)	17.0		42.0	0.40‡
Mild/moderate/proliferative (%)	2.7		16.3	
Nephropathy (33)	*N* = 2,885		*N* = 374	
Elevated ACR ≥30 μg/mg (%)	9.2		22.2	<0.0001‡
Neuropathy	*N* = 329		*N* = 70	
Peripheral neuropathy MNSE >2 (%) (35)	8.2		25.7	<0.0001‡
Heart rate variability (%) (36)	−11.6	0.003††		
Arterial stiffness (37)	*N* = 535		*N* = 60	
Pulse wave velocity (m/sec)	5.3		6.4	<0.01‡
BrachD (%/mmHg)	6.1		5.2	<0.01‡

ACR, albumin/creatinine ratio; BrachD, brachial distensibility (lower is stiffer); CVD, cardiovascular disease; MNSE, Michigan neuropathy screening examination; pulse wave velocity, carotid to femoral (higher is stiffer). *Within type of diabetes. †Hypertension: diastolic blood pressure ≥90th percentile for age, sex, and height or taking medication for high blood pressure; triglycerides ≥110 mg/dL; HDL ≤40 mg/dL; waist ≥90th percentile for age, sex, and height; apoB ≥100 mg/dL; dense LDL, relative flotation rate ≤0.237. ‡Between type of diabetes. ††Compared with nondiabetic control subjects, *N* = 354 type 1; 176 control subjects.

high-risk populations to delay the long-term impact of these complications.

While Many Youth With Diabetes Are Receiving Quality Care, a Significant Proportion of Youth Who Are Racial/Ethnic Minorities and "Emerging Adults" Are Not

Optimal care is an important component of successful long-term management for youth with diabetes. While there are high levels of adherence for some diabetes care indicators such as blood pressure checks (95%), urinary protein tests (83%), and lipid assessments (88%), approximately one-third of youth had no documentation of eye or A1C values at appropriate intervals and therefore were not meeting the American Diabetes Association (ADA)-recommended screening for diabetic control and complications (40). Participants ≥18 years old, particularly those with type 2 diabetes, and minority youth with type 1 diabetes had fewer tests of all kinds performed. Challenges in the transition from pediatric to adult care were also observed. There was a ~2.5 times greater odds of poor glycemic control among youth with type 1 transitioning to adult care compared with those who remained in pediatric care, suggesting that this period requires a high level of support to ensure success (41). Importantly, using basal-bolus therapies and higher frequency of glucose monitoring were associated with lower A1C in youth with type 1 diabetes (42).

These data highlight the challenges associated with achieving recommended goals for appropriate diabetes management in youth and indicate that some subgroups are particularly vulnerable.

A Simple Etiologic Classification of Diabetes Type Is Possible for Youth-Onset Diabetes

Because recognition of the broader spectrum of diabetes in children and adolescents is recent, there are no gold-standard definitions for differentiating the types of diabetes in this population, either for research or clinical purposes or for public health surveillance. The ADA classification of diabetes as type 1 and type 2 does not include operational definitions for the specific etiologic markers of diabetes type, such as types and numbers of diabetes autoantibodies or measures of insulin resistance, hallmarks of type 1 and 2 diabetes, respectively (43). Moreover, obese adolescents with a clinical phenotype suggestive of type 2 diabetes can present with ketoacidosis (44) or have evidence of autoimmunity (45).

Using the ADA framework (43), we operationalized definitions of two main etiologic markers, autoimmunity and insulin sensitivity, to identify four etiologic subgroups based on the presence or absence of markers. Autoimmunity was based on presence of one or more diabetes autoantibodies (GAD65 and IA2). Insulin sensitivity was estimated using clinical variables (A1C, triglyceride level, and waist circumference) from a formula that was highly associated with estimated insulin sensitivity measured using a euglycemic-hyperinsulinemic clamp among youth with type 1 and 2 and normal control subjects (46). Participants were categorized as insulin resistant (estimated insulin sensitivity <8.15, representing the lowest 25th percentile among National Health and Nutrition Examination Survey youth) and insulin sensitive (47). Using this approach, 54.5% of SEARCH cases were classified as typical type 1 (autoimmune, insulin-sensitive) diabetes, while 15.9% were classified as typical type 2 (nonautoimmune, insulin-resistant) diabetes. Cases that were classified as autoimmune and insulin-resistant likely represent individuals with type 1 autoimmune diabetes and concomitant obesity, a phenotype becoming more prevalent as a result of the recent increase in the frequency of obesity, but is unlikely to be a distinct etiologic entity. This is supported by the following: *1*) the phenotype represented ~26% of all autoimmune cases, a proportion similar to that expected, given that the definition of insulin resistance was based on the lowest 25th percentile for the National Health and Nutrition Examination Survey, and *2*) there was a similar prevalence and titers of diabetes autoantibodies

and similar distribution of HLA DR-DQ risk genotypes to those observed in the typical type 1 case (autoimmune and insulin sensitive), suggesting a similar contribution of immune-mediated disease processes (47).

Ten percent of SEARCH participants had no evidence of either autoimmunity or insulin resistance and thus require additional testing, including additional measurements of diabetes-related autoantibodies (only two antibodies were measured in SEARCH) as well as testing for monogenic forms of diabetes to clarify etiology. Among antibody-negative youth, 8% of those tested had a mutation in one or more of the hepatocyte nuclear factor-1α (HNF-1α), glucokinase, and HNF-4α genes, an estimated monogenic diabetes population prevalence of at least 1.2% (48).

These findings allowed us to propose a straightforward clinical classification scheme (Fig. 3) without a requirement for a new etiologic category (i.e., type 1.5 or double diabetes). With some additional clinical data collection (especially antibodies and waist circumference), the vast majority of cases can be readily classified.

A summary of major topics and references from SEARCH and the ancillary studies is shown in Table 2.

Future Challenges and Opportunities

SEARCH has begun to clarify gaps in the understanding of diabetes among youth but challenges remain. Type 1 diabetes is not uncommon among minority youth as previously assumed, and type 2 diabetes is diagnosed among youth from all racial/ethnic groups. Both type 1 and type 2 diabetes are increasing over time, signaling a major challenge for the provision of health care resources. While recent evidence suggests that obesity rates may be plateauing among youth (49), this will at best result in a future plateauing of the rates of type 2 diabetes in this population, though not necessarily disease burden. A recent analysis suggests that given current population projections and observed trends, the number of youth with type 1 diabetes will nearly triple and type 2 diabetes prevalence will quadruple by 2050 (50).

Continued surveillance is needed to answer important questions:

- Will type 1 diabetes incidence continue to rise across all race and ethnicity groups in the U.S., or will there be a leveling off, as recently reported in Scandinavia (51–53)?
- Will type 2 diabetes incidence rise across all race and ethnicity groups in the U.S., or will there be a plateauing as obesity rates plateau?

Challenges to "sustainable" surveillance (e.g., relatively inexpensive, rapid, and more geographically diverse) must be faced. There is frequent movement of youth with diabetes between health care providers and systems over short time spans, making ascertainment, especially of type 2 diabetes, surprisingly difficult. While implementation of electronic health record (EHR) systems is rapidly occurring, the harmonization of multiple data systems and the identification of crucial information (e.g., date of diagnosis and type of diabetes) remain difficult (54). Absence of testing for diabetic antibodies and measurement of waist circumference are also common and limit the use of existing records. The increasing use of EHRs may permit easier surveillance, but substantial work remains to realize significant efficiencies.

The SEARCH cohort study was designed to explore the clinical evolution of diabetes and its complications on a sample of youth with type 1 and type 2 diabetes in contemporary care. Despite current treatment options, the prevalence of poor glycemic control is high, particularly among minority youth. Our initial findings suggest that a substantial number of youth with diabetes will develop serious, debilitating complications early in life, which is likely to have significant implications for their quality of life, as well as economic and health care implications. An especially high burden was noted among youth with type 2 diabetes, consistent with data from the TODAY study (55–57), and youth of minority racial/ethnic groups. Therefore, important questions remain:

- Are diabetic complications more frequent in youth with type 2 than type 1 of similar race/ethnicity and diabetes duration? Are such complications more frequent in minority youth regardless of diabetes type?
- Are there differences in the onset, diabetes duration, and clustering of complications between type 1 and type 2 diabetes?
- Do known risk factors explain observed differences or must other factors be identified?
- Are the sequence and severity of diabetic complications similar in youth with type 1 and type 2 diabetes, or are different mechanisms involved?
- What will the impact be of the Affordable Care Act implementation on the care of youth and young adults with diabetes, particularly those with type 2 diabetes?

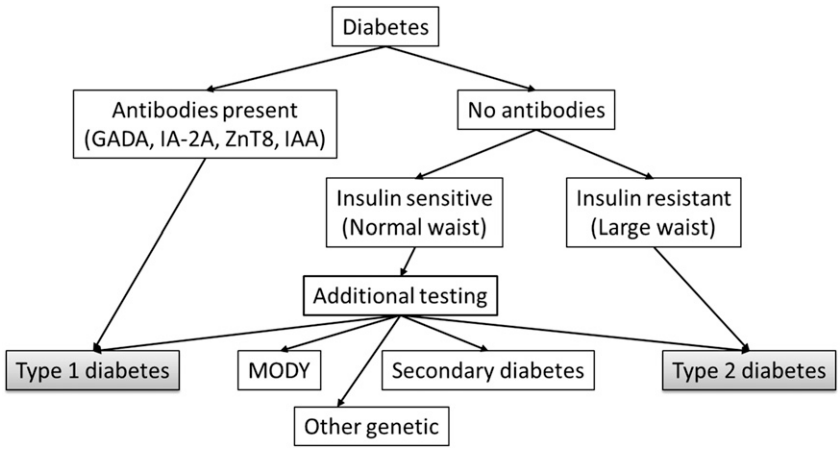

Figure 3—Proposed algorithm for classification of pediatric diabetes. Presence of any antibodies indicates type 1 diabetes. Absence of antibodies and a large waist [or insulin sensitivity score $<$8.15 units (47)] indicates type 2 diabetes. Individuals with no antibodies and a normal waist (or insulin sensitivity score $\geq$8.15 units) require additional testing for potential monogenic forms of diabetes or other defects. GADA, GAD antibody; IAA, insulin autoantibody; MODY, maturity-onset diabetes of the young.

Table 2—Major topics and papers from the SEARCH study and ancillary studies*

- Burden of diabetes (prevalence/1,000)
  - 2001 (5); 2009 (6); changes in prevalence 2001–2009 (2); projections of diabetes burden to 2050 (50)
- Risk of diabetes (incidence/100,000)
  - 2002 to 2003 (12); 2008 to 2009 (13); trends in incidence, non-Hispanic whites (2002–2009) (14)
- Race/ethnicity–specific characteristics
  - Navajo (21); Asian, Pacific Islander (23); Hispanic (22); African American (24); non-Hispanic white (20)
- Adiposity
  - Prevalence of overweight and obesity (25)
  - Weight-loss practices and weight-related issues (58)
- Clinical, biochemical, and genetic findings
  - Glycemic control
    - Lipids and glycemic control (59)
    - Glycemic control and change in lipids (61)
    - Psychosocial burden and glycemic control (63)
  - HLA and genetics
    - HLA-associated phenotypes (60)
    - Time trends in HLA susceptibility among type 1 in Colorado (62)
    - Prevalence of MODY due to HNF1A, HNF4A, glucokinase (48), JDRF Monogenic Study*
    - Prevalence of permanent neonatal diabetes (64), JDRF Monogenic Study*
    - TCF7L2 and type 2 in multiethnic youth (66)
  - β-Cell function
    - Preservation of β-cell function in autoantibody positive youth (65)
    - Evolution of β-cell function (67)
    - Testing the accelerator hypothesis: body size, β-cell function, age at onset among type 1 (68)
  - Type of diabetes
    - Development of an insulin sensitivity score (46)
    - Etiologic approach to characterization of diabetes type (47)
  - CVD risk factors
    - CVD risk factor clustering (69)
    - Prevalence of elevated apoB and small, dense LDL (32)
    - Lipids among type 1 and control subjects (71), SEARCH CC*
    - CVD risk factors among type 2 and controls (73), SEARCH CC*
    - Prevalence of tobacco use and CVD risk factors (75)
- Developmental origins
  - Maternal diabetes in utero and age at diagnosis among type 2 (70)
  - Maternal obesity and diabetes in utero and type 2 (72), SEARCH CC*
  - Breast-feeding and type 2 in three ethnic groups (74), SEARCH CC*
- Behavioral factors
  - Physical activity and self-concept (76), SEARCH CC*
  - Physical activity and electronic media use (26), SEARCH CC*
  - TV and computer use (79)
  - Cardiovascular health among type 1 (81), SEARCH CVD*
- Nutrition
  - Dietary intake (27)
  - Correlates of dietary intake (77)
  - DASH diet and CVD risk factors (78)
  - Change in DASH diet and CVD risk factors (80)
  - Sugar sweetened beverages and CVD risk profile (82)
  - DASH diet and hypertension (83)
  - Vitamin D insufficiency prevalence and association with insulin resistance (85), SNAS*
  - Nutritional factors and preservation of C-peptide among type 1 (87), SNAS*
  - Fructose intake and CVD risk factors among type 1 (89), SNAS*
  - Dietary intake patterns and arterial stiffness (91), SNAS* and CVD*
- Quality of life
  - Health-related quality of life (84)
  - Demographic and clinical correlates of quality of life among type 1 (86)
  - Longitudinal associations among sex, self-care, and quality of life (88)
  - Prevalence and correlates of depressed mood (90)
  - Metabolic and inflammatory links with depression (92)

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CONCLUSIONS

Our findings to date have contributed to a better understanding of the complex nature of diabetes in youth; however, the increasing trends in the burden of type 1 and type 2 diabetes suggest that there is a pressing need to continue high-level, comprehensive surveillance efforts. Given the evidence of early complications despite current therapeutic approaches, continuing long-term follow-up of youth with diabetes is necessary to expand our understanding of its natural history, so the most appropriate approaches to primary, secondary, and tertiary prevention of diabetes and its complications in youth can occur.

A listing of all SEARCH publications is available at www.searchfordiabetes.org. The Supplementary Data lists the SEARCH investigators and staff at each of the sites.

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Table 2—Continued

Acute complications
Prevalence of DKA at onset (19)
Trends in DKA at onset (44)
Risk factors and early complications
Carotid structure and function among type 1 (39), SEARCH CVD*
CVD risk factors associated with increased arterial stiffness among type 1 (93), SEARCH CVD*
Smoking and arterial stiffness among type 1 (95), SEARCH CVD*
Reduced HRV in type 1 and control subjects (36), SEARCH CVD*
Glycemic control and HRV (94), SEARCH CVD*
Reduced HRV is associated with increased arterial stiffness among type 1 (96), SEARCH CVD*
Quality of care
Barriers to care among type 1 (97)
Treatment patterns among type 2 (99)
Transition from childhood to adult care among type 1 (41)
Insulin regimens and clinical outcomes (42)
Predictors of insulin regimens among type 1 (102)
Spatial epidemiology and built environment
Neighborhood level risk factors among type 1 (98), SPATIAL*
Geographic variation in type 1 and 2 in four U.S. regions (100)
Surveillance
Ascertainment of diabetes using EHRs (54,101)
Adherence to treatment guidelines (40)

Studies shown in Table 1 are not included in Table 2. CVD, cardiovascular disease; DASH, Dietary Approaches to Stop Hypertension; HRV, heart rate variability. *Ancillary studies include SEARCH Case-Control (CC); SEARCH CVD; Juvenile Diabetes Research Foundation (JDRF) Monogenic Study; SEARCH Nutrition Ancillary Study (SNAS); and SEARCH Spatial Epidemiology of Diabetes (SPATIAL).

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