Sociodemographic Associations of Longitudinal Adiposity in Youth with Type 1 Diabetes

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Abstract

Excess adiposity is common in youth with type 1 diabetes, yet little is known about the sociodemographic factors that predict longitudinal trajectories of body fat. We analyzed data from 363 females and 379 males with type 1 diabetes over ~9 years of follow-up (mean baseline age 12.8 ± 2.3 in females, 13.2 ± 2.4 in males). Estimated body fat percentage (eBFP) was calculated with validated sex- and race/ethnicity-specific equations. Group-based modeling identified three eBFP trajectories for each sex. All female trajectories showed gradual increases while male trajectories showed gradual decreases (<5% in eBFP) that plateaued around 7 years of diabetes duration. Female trajectories showed differences in baseline eBFP: Group F1 (38.0%), mean eBFP 27.8±3.0%; Group F2 (47.9%), mean eBFP 33.9±3.0%; Group F3 (14.1%), mean eBFP 41.7±4.1%. Male trajectories also showed differences in baseline eBFP: Group M1 (57.2%), mean eBFP 22.0±3.0%; Group M2 (30.9%); mean eBFP 33.9±3.0%; Group M3 (12.9%), mean eBFP 36.1±3.7%. In multinomial models adjusted clinical factors (e.g. insulin regimen, insulin dose, and hemoglobin A1c), females who reported a single-parent household (adjusted OR (aOR)=3.34, 95% CI 1.49, 7.47), parental education of less than a college degree (aOR=3.79, 95% CI 1.60,

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9.60), and a lack of private health insurance (aOR=3.74, 95% CI 1.45, 9.60), and a household income of less than $75,000 per year (aOR=3.13 (95% CI 1.27, 7.70) were approximately 3–4 times more likely to be in the highest eBFP trajectory group relative to the lowest eBFP trajectory group. Males who reported a household income <$75000/year were almost twice as likely to be in Group M3 than Group M1 in the unadjusted model only (aOR=1.79, 95% CI 0.91, 4.01 versus unadjusted OR: 2.48, 95% CI 1.22, 5.06). Lower socioeconomic status may be associated with excess body fat throughout adolescence in type 1 diabetes, particularly among females.

Keywords

Diabetes mellitus, type 1; Adolescent; Adiposity

Introduction:

The prevalence of obesity in youth and young adults with type 1 diabetes now parallels that of the general population, while the prevalence of overweight is even higher[1,2]. Together approximately 36% of adolescents with type 1 diabetes are currently overweight/obese. Obesity in childhood and adolescence is associated with a host of negative health consequences, including increased inflammation, insulin resistance, dyslipidemia, and oxidative stress, all of which increase the risk for adverse cardiovascular disease events[3,4]. Among individuals with type 1 diabetes, the cardiovascular disease risk that is associated with excess adiposity is superimposed on a diabetes-related baseline risk that is already elevated up to 10-fold as compared to the general population[5–7].

Weight status represents a complex interaction of biological, behavioral, and cultural factors[8]. Day-to-day management of type 1 diabetes includes a strict regimen to prevent future macro-and microvascular complications associated with the disease[9], including dosing insulin and responding to episodes of hypoglycemia with appropriate intake of rapid-acting carbohydrates. As such, there are also unique clinical factors specific to type 1 diabetes management that are associated with increased adiposity[10]. Intensified insulin therapy, while effective in preventing diabetic complications, is associated with weight gain[11,12]. This effect has been attributed to decreased glucosuria[13,14], increased caloric intake to treat hypoglycemia[15,16], and increased lipogenesis associated with hyperinsulinemia[13,17]. Modern therapeutic technologies used for intensive insulin therapies[18], such as insulin pumps, may further drive weight gain due to increased dietary flexibility[19,20], although this relationship remains controversial[21]. Epidemiologic studies reveal that increased adiposity in type 1 diabetes is associated with longer diabetes duration[10,22] and higher insulin dose[10,19]. Despite presumed glucosuria, higher BMIz is also associated with elevated hemoglobin A1c (HbA1c) levels[10,23], which may be a reflection of increased insulin resistance at higher body weight[24].

In the general population, the prevalence of pediatric obesity varies by race and ethnicity[25,26] and socioeconomic factors[27], suggesting that health inequity may be an important predictor of unhealthy weight status early in life. Similar demographic correlates of excessive weight gain have also been implicated in type 1 diabetes, as it has been shown

that youth who are of Hispanic ethnicity are at the highest risk of being overweight or obese[10]. Additional socioeconomic correlates of overweight/obese status among youth with type 1 diabetes include lower household income[10,28] and lower parental education level[22].

Understanding the common patterns, or trajectories, of weight gain through childhood and adolescence could help to identify the youth with type 1 diabetes who may be most susceptible to unfavorable changes in adiposity[29]. However, the longitudinal studies to date have primarily focused on weight status in terms of body mass index (BMI) z-score[2] and over short time periods within the first year of diagnosis[30] or among youth with > 1 year T1D duration [28]. Here, we set out to address these gaps related to longitudinal trends and predictors in adiposity in youth with type 1 diabetes. Because BMI is limited in its ability to describe changes in fat mass[31], we used validated predictive equations to estimate body fat percentage[32]. Our objectives were to identify subgroups of youth with type 1 diabetes who follow the same trajectories of body fat percentage and to study how sociodemographic characteristics (i.e. race and socioeconomic status) and clinical factors (i.e. insulin regimen, insulin dose, and glycemic control) were associated with each subgroup. Given that youth with type 1 diabetes are free-living individuals who interact with the same obesogenic environment and aspects of health inequity as youth without type 1 diabetes, we then tested if there were baseline sociodemographic associations with longitudinal adiposity that operate independent of clinical drivers of weight gain specific to type 1 diabetes.

RESEARCH DESIGN AND METHODS:

Study population

The SEARCH for Diabetes in Youth Study, began in 2000 with an overarching objective to describe the incidence and prevalence of childhood diabetes among the five major race and ethnic groups in the U.S, including non-Hispanic white, Hispanic, Asian/Pacific Islander, African American, and American Indian[33]. Children and adolescents with diabetes diagnosed < 20 years of age were identified from a population-based incidence registry network at five U.S. sites (South Carolina, Cincinnati, Ohio and surrounding counties, Colorado with southwestern Native American sites, Seattle, Washington and surrounding counties, and members of Kaiser Permanente, Southern California in 7 counties) by the SEARCH for Diabetes in Youth Registry Study[34]. Cases were newly diagnosed with type 1 diabetes in 2002–2006 or 2008 and were identified from on-going surveillance networks of hospitals and health care providers. Individuals who could be contacted were recruited for a baseline research visit (mean of 9.0± 6.3 months after diagnosis of type 1 diabetes), and if completed, asked to return for visits at 12, 24, and 60 months to measure risk factors for diabetes complications (Figure 1, Panel A). A subset of participants who had at least five years of diabetes duration, aged 10 years and older, were recruited for a follow-up 'cohort' visit between 2012–2015.

Inclusion criteria for these analyses consisted of youth diagnosed with type 1 diabetes between 2002 and 2005, as these incident years were invited for all subsequent major measurement visits (12-month, 24-month, 60-month and follow-up visits and the cohort visit). Type 1 diabetes was based the clinical diagnosis (of type 1a, type 1b, or type 1 diabetes) made by their physician or other health care provider, abstracted from medical

charts. Youth who were younger than 10 years old at baseline were excluded as eBFP estimation equations are validated for those who are ages 10 and older (n=945). Youth were also excluded if they were greater than 300 pounds (136.4 kilograms) or taller than 6.5 feet (1.96 meters) at any visit as these individuals were not included in the original DEXA study (n=0 females, n=4 males). Youth who had fewer than three measures of eBFP (see below) of follow-up were excluded (n=269). The final study sample included 742 youth with type 1 diabetes (363 females and 376 males, see Figure 1, Panel B). The study was approved by Institutional Review Boards with jurisdiction, and the parent, adolescent or young adult, or both provided written consent or assent for all participants.

Research visits

Trained personnel administered questionnaires, made measurements of height, weight, and blood pressure and obtained blood samples. Body mass index (BMI) was defined as weight (kilograms) divided by height (meters^2) and converted to a Z score[35]. Waist circumference was measured using the natural waist location and was used to calculate waist to height ratio. A blood draw occurred after an 8 hour overnight fast, and medications, including short-acting insulin, were withheld the morning of the visit.

Laboratory measures

Blood samples were obtained under conditions of metabolic stability, defined as no episodes of diabetic ketoacidosis in the preceding month and the absence of fever and acute infections. They were processed locally and shipped within 24 hours to the central laboratory (Northwest Lipid Metabolism and Diabetes Research Laboratories, Seattle, WA). HbA1c was measured by a dedicated ion exchange high–performance liquid chromatography instrument (TOSOH Bioscience).

Other measures

Self-reported race and ethnicity were collected using questions from the 2000 US Census[36]; available choices were non-Hispanic white, non-Hispanic African American, Hispanic, and "Other" (Asian American, Native American, Asian Pacific Islander, Other, and Unknown). Health insurance type was classified as private, Medicaid or Medicare, or none/other. Parental education was based on the highest educational level attained by either parent and classified as less than high school degree, high school graduate, some college through associate degree, and bachelor's degree or more. Household structure was classified as two-parent household or single-parent household.

Insulin regimen was based on mode of insulin delivery (i.e., insulin pump, syringes, insulin pen devices) and classified as pumps, long-acting with rapid-acting insulin injections with 3 or more injections per day, and any other form of multiple daily injections (Long + Other Combination, 2+ Times/Day OR Any Insulin Combination (excluding Long), 3+ Times/Day OR Any Insulin(s) taken 1×/Day, or any Insulin combination (excluding Long) 2+/Day. Insulin dose was reported as total daily dose standardized per kilogram of body weight. For multinomial modeling, insulin regimen was reclassified as a binary variable due to small cell sizes (pumps and long-acting with rapid-acting insulin injections with 3 or more injections per day versus any other form of multiple daily injections (Long + Other Combination, 2+

Times/Day OR Any Insulin Combination (excluding Long), 3+ Times/Day OR Any Insulin(s) taken 1×/Day, or any Insulin combination (excluding Long) 2+/Day). Frequency of self-blood glucose monitoring was self-report and classified as <1 time per day, 1–3 times per day, and 4 times per day.

Outcome Definition: eBFP

While BMI is a well-known indicator of health risks associated with increased weight, it is known to be limited in its ability to purely describe adiposity changes[31,37]. Therefore, we used validated equations developed from 1999–2006 NHANES to predict percent body fat percentage measurement in Americans 8 years and older[32] were used to generate a new variable: estimated body fat percentage (eBFP). Equations are shown in Supplemental Table S1.

Equations incorporate age, race, weight, height, and waist circumference. Equations are sex- and race/ethnicity-specific (White, Black, Mexican-American, and "Other"). Participants who identified as Hispanic and also reported that they were Mexican American were modeled with the Mexican American equation; all other Hispanics were modeled with the "Other" equation[32].

Group-Based Trajectory Modeling

We used group-based trajectory modeling to identify longitudinal trajectories of eBFP among youth with type 1 diabetes using the SAS PROC TRAJ procedure (v9.4, SAS Institute, Cary, NC) which fits a semi-parametric (discrete mixture) model for longitudinal data using the maximum-likelihood method[38–40]. Details about trajectory analysis have been described elsewhere[41,42]. eBFP trajectories were modeled in terms of disease duration (months since baseline visit) to visualize possible changes in body fat associated with the course of type 1 diabetes. Due to the sex-specific changes in body composition that occur during puberty, eBFP trajectories groups were stratified by sex.

The optimal number of trajectory groups was determined based on Bayesian Information Criterion (BIC) (i.e. smallest absolute value) and having at least 5% of the sample in the smallest trajectory group. Each participant was then assigned to the eBFP trajectory group with the largest Bayesian posterior probability (BPP) of group membership. We then used the assigned values of eBFP group membership as outcomes in regression modeling.

Multinomial Regression Modeling:

Multinomial regression was used to assess the association of five key sociodemographic characteristics with the eBFP trajectory groups, adjusing for baseline variables. Separate models were fit to assess race/ethncity (Non-Hispanic white versus non-white), family structure (2-parent household versus single-parent household structure), maximum parent education (attainment of a bachelors degree or higher versus less than a bachelors degree), health insurance type (private health insurance versus public, other, or no insurance), and household income level ($75K per year versus <$75K per year). Model 1 was unadjusted. Model 2 was adjusted for age at diagnosis and clinic site and clinical drivers of weight (insulin dose, insulin regimen, and HbA1c). Model 3 was fully adjusted and included all

sociodemographic exposures. Multiple comparisons in the overall tests of difference were corrected for the positive False Discovery Rate[43] (pFDR) and q-values are reported[43].

All analyses were completed in SAS software and used a two-sided - value or q-value of 0.05 to indicate statistical significance. Descriptive analyses used the mean and standard deviation (SD), or median and interquartile range (IQR) for non-normal distributions, for continuous variables and frequencies to describe categorical variables. The means and frequencies of demographic and clinical characteristics were compared using chi-square for categorical and ANOVA or Kruskal-Wallis for continuous variables.

RESULTS

Trajectory Modeling

The analysis included 363 females and 376 males with type 1 diabetes. Table 1 depicts the baseline characteristics of the study sample, stratified by sex. Mean age at baseline was 12.8 ± 2.3 years in females and 13.2 ± 2.4 years in males. Mean type 1 diabetes duration at baseline visit was 9.7 ± 6.6 months for females and 9.5 ± 6.4 months for males. Group-based trajectory modeling identified three eBFP trajectories in females shown in Figure 2A. All female trajectories showed gradual increases in eBFP that plateaued by approximately 7 years of diabetes duration. Distinct trajectories were defined by differences in baseline eBFP: Group F1 (38.0%) had the lowest eBFP (mean baseline eBFP: 27.8±3.0%); Group F2 (47.9%) had a moderate eBFP (mean baseline eBFP: 33.9±3.0%), and Group F3 (14.1%) had the highest eBFP (mean baseline eBFP: 41.7±4.1%). Distinct male trajectories are shown in Figure 2B. All male trajectories showed gradual decreases in eBFP that plateaued by approximately 7 years of diabetes duration. Distinct trajectories were defined by differences in baseline eBFP: Group M1 (57.2%) had the lowest eBFP (mean baseline eBFP: 22.0±3.0%), Group M2 (30.9%) had a moderate eBFP (mean baseline eBFP: 29.2±4.1%), and Group M3 (12.0%) had the highest eBFP (mean baseline eBFP: 36.1±3.7%). As compared to males, female youth and adolescents with type 1 diabetes exhibited higher estimated body fat percentage at baseline and showed an increase in percentage body fat over ~9 years of follow-up. By contrast, males with type 1 diabetes showed a decrease in estimated body fat percentage over the same period.

Associated Sociodemographic Factors

In females, the highest eBFP trajectory group included the highest prevalence of non-white youth and youth from single-parent households, a lower level of parental educational attainment, and a lack of private health insurance at baseline (p<0.05 see Table 1A). This group also had the highest mean HbA1c at baseline. Table 2A depicts the odds ratios (OR) for each of five sociodemographic exposures and eBFP trajectory group in an unadjusted model and a model adjusted for baseline confounders (e.g. age at diagnosis, clinic site) and clinical factors (e.g. insulin regimen, insulin dose, and HbA1c). Females who reported a single-parent household (adjusted OR (aOR)=3.34, 95% CI 1.49, 7.47), parental education of less than a college degree (aOR=3.79, 95% CI 1.60, 9.60), and a lack of private health insurance (aOR=3.74, 95% CI 1.45, 9.60), and a household income of less than $75,000 per year (aOR=3.13 (95% CI 1.27, 7.70) were approximately 3–4 times more likely to be in the

highest eBFP trajectory group relative to the lowest eBFP trajectory group. After adjustment for clinical factors, non-white race was no longer associated with membership in the highest eBFP group. In the final model including all sociodemographic variables, household income was dropped due to multicolllinearity with other variables. A single-parent household and lower levels of parental education were associated with membership in the highest eBFP trajectory group (aOR of single-parent household in Group F3 versus Group F1: 2.45, 95% CI 1.01, 5.97; aOR of parental education less than a college degree in Group F3 versus Group F1: 2.54, 95% CI 1.00, 6.44.)

In males, the highest eBFP trajectory group included the highest prevalence of youth who reported low levels of annual household income (p<0.015, see Table 1B). Although household income remained significantly associated with eBFP trajectory group, the association was attenuated with adjustment for baseline clinical factors for the highest eBFP trajectory group (aOR of household income <$75,000 per year in Group M3 versus Group M1: 1.79, 95% CI 0.91, 4.01 versus unadjusted OR: 2.48, 95% CI 1.22, 5.06) but not the moderate eBFP trajectory group (aOR of household income <$75,000 per year in Group M2 versus Group M1: 1.70 95% CI 1.01, 2.88 versus unadjusted OR 1.93, 95% CI 1.20, 3.09; see Table 2B). In the final model including all sociodemographic variables (Model 3), health insurance status and income were highly collinear. Household income was retained because it was significant in Model 2 while health insurance status was not. In this final model, no sociodemographic variables were associated with membership in the highest eBFP trajectory groups among males.

DISCUSSION

In a large, population-based cohort of youth with type 1 diabetes, we found three distinct trajectories of adiposity by sex over a mean follow-up of approximately nine years. While in females all three trajectories had positive slopes, in males they all had negatives slopes. Our findings emphasize sex-specific changes in body composition over adolescence and into adulthood, as well as sex-specific determinants of excess adiposity among youth with type 1 diabetes.

Compared to male trajectory groups, female trajectory groups showed higher intercepts and more positive slopes over follow-up time. In healthy children, females tend to have more body fat than males for the same Tanner stage of puberty[44,45]. Multiple studies have also shown that females with type 1 diabetes are more likely to be overweight and/or obese than males with type 1 diabetes[10,22,28,46]. Here, we corroborate that females have higher percentage body fat than males at a mean age of 21.0 ± 2.7 years for females and 21.4 ± 2.6 years for males, at which time puberty and linear growth is generally complete. Given the mean age at baseline (~10 years) and nine years of subsequent follow-up, the sex-specific slope of eBFP trajectories likely reflects normal changes in body composition associated with puberty, where sex hormones lead to increased body fat in females and decreased body fat in males[45].

An important finding of the trajectory analysis was that the rate of change of eBFP was fairly uniform across sex-specific subgroups. In both sexes, baseline eBFP was a significant

predictor of trajectory group (i.e. the slopes did not cross). Since the baseline visit occurred on average ~10 months after they were diagnosed with type 1 diabetes, these results could indicate that weight status within the first 6 months of diabetes diagnosis is an important predictor of longitudinal adiposity. This finding conflicts with data from a small clinical study which showed that girls with type 1 diabetes were leaner at diagnosis and 1 year following diagnosis as compared to males, suggesting that obesity in females may onset later in the disease course[47].

The trend in age at diagnosis and eBFP group was different in males and females, where girls who are diagnosed at an older age (approximately 13 years) are more likely to be in the highest eBFP group, while males who are diagnosed at an older age are more likely to be to be in the lowest eBFP group. One possible explanation for this could be that many females will have already experienced their pubertal growth spurt by the age of 13 years, while more males may be just beginning puberty-related growth at that age. Therefore, females may begin taking insulin at a time in which energy expenditure is lower than earlier stages of puberty and anabolic effects are more pronounced, leading to increased fat storage[48]. By contrast, males may begin taking insulin around a time in which the anabolic effects coincide with energy needed for linear growth spurts[18,44]. Differences in dietary habits and exercise activities of boys versus girls in late stage of puberty might also explain different eBFP[16].

In females with type 1 diabetes, the highest eBFP trajectories were associated with a higher HbA1c level at baseline. Although epidemiological evidence suggests population-level associations between excess adiposity and higher HbA1c[2], the literature on HbA1c and body fat in females is conflicting[28,49]. In this age range, our results may be reflective of earlier puberty onset and its associated insulin resistance that may challenge glycemic control[50]. This effect is partially attributed to elevated growth hormone[51]. There are also reports that pubertal insulin resistance is more marked in females than males due to accumulation of visceral fat[52].

In females with type 1 diabetes, proxies of lower socioeconomic status including household structure, parental education, health insurance type, and household income individually predicted membership in the higher eBFP trajectory groups. These findings are consistent with the general population, where the incidence of childhood obesity is associated with lower household and community income levels[27,53] lower parental education[38], and living in multiple-households[54]. Critically, this effect appears to be independent from the effect of clinical drivers of weight gain as evidenced by significant associations after adjustment for those factors. In males with type 1 diabetes, household income level was the sole sociodemographic factor associated with longitudinal eBFP trajectory group.

In a final model including all sociodemographic correlates, single-parent households and lower parental education emerged as associations with longitudinal adiposity in females only. A previous study found that time-varying BMI was inversely related to household income among youth with T1D of both sexes [28]. It is possible that small to moderate correlation between the sociodemographic variables in Model 3 (Pearson's correlation coefficients ranging from 0.2–0.3) may have also attenuated statistical significance in the

final model. Further research may be warranted to investigate the reasons why markers of health inequity are stronger risk factors for increased adiposity among females with type 1 diabetes as compared to males and if there are sex-specific mediators of these associations. For example, there may be more marked psychosocial variation (i.e. depressive symptoms[55]) or behavioral patterns (i.e. aberrant eating behaviors[56,57]) that may play into weight changes among females with type 1 diabetes who are affected by racial or socioeconomic disparity.

Above all, our findings reinforce that youth with type 1 diabetes are susceptible to unfavorable body composition based on the same sociodemographic aspects as the general pediatric population. Although the specific associations with eBFP trajectory group were different across sex, we found evidence that multiple sociodemographic correlates may be important predictors of longitudinal adiposity among this population. Obtaining accurate assessments of cultural, financial, or educational barriers to weight management, including healthy eating and physical activity, may be crucial to identify specific behaviors to target for change[58]. Future weight management interventions for type 1 diabetes may be more effective if they integrate clinical and behavioral recommendations with demographic information and socioeconomic status to understand patient-specific barriers to health weight.

Our study has several limitations. eBFP is a proxy for body fat and the predictive equations were derived and validated in the general population[32]. Although we expect minimal differences in the relationship between anthropometric variables and estimated body fat percentage among young people with type 1 diabetes, it would be ideal to validate equations in this population. We used this measure as an indicator of adiposity in the place of BMI, as BMI is not a precise indicator of the underlying proportion of fat and lean tissue[59]. In exploratory analyses, we examined sex-specific trajectories of BMI (which is a more appropriate measure than z-score or percentile when analyzing changes over time[60]) and assessed how BMI-derived subgroups agreed with eBFP trajectory subgroups groups. In both sexes, BMI trajectories increased over the follow-up duration (See Supplemental Figure 1). The inverse relationship between body fat percentage and BMI among males, but not females, in our study sample is consistent with previous longitudinal studies in the general population documenting complex relationships between body fat percentage and BMI depending on sex, where negative changes in body fat percentage occurred with concurrent increases in BMI percentile among males ages 13 to 18 years[61]. By contrast, the parallel trends in females reinforces other reports that that BMI may be a more accurate assessment of fatness in females[62,63]. We also found strong agreement between the *relative* classification of eBFP and BMI subgroups among females and reasonable agreement among males (Supplemental Table S2). The highest misclassification occurred among males in the moderate eBFP trajectory group (M2) with higher agreement in the lowest and highest ebFP groups.

Other limitations include residual confounding that may result from the race-specific equations used to calculate eBFP, in which multiple races and cultures were grouped into a single category. Our trajectories are modeled in terms of disease duration; the advantage of this approach is that it displays body fat trajectory in the early natural history of type 1 diabetes. However, these models cannot be directly compared to age- and sex- specific body

fat trajectories in populations without type 1 diabetes. Here, we study baseline associations with trajectory group membership. Variables measured at baseline may be time varying, such as health insurance status, insulin regimen, and insulin dose. Separate analytic methods such as multilevel modeling may be more well-suited to directly assess the association between time-varying clinical factors such as insulin intensification and changes in body composition over time. However, the majority of key sociodemographic associations are likely to remain constant over follow-up including race/ethnicity, parental education, and household structure. Finally, a larger sample may identify additional trajectories that capture the experience of smaller subpopulations, such as individuals who show more rapid increases (or decreases) in eBFP over the first nine years of T1D.

Our study also has several strengths. Group-based trajectory modeling is a novel approach to understand overweight and obesity within the SEARCH for Diabetes in Youth cohort as clusters of individuals that follow a similar developmental trajectory over time. With a large cohort size and diverse patient population, the SEARCH for Diabetes in Youth Study provides a robust data set from which to identify common trajectories eBFP in youth and young adults with type 1 diabetes and discern the sociodemographic and clinical variables associated with each major trajectory. By integrating sociodemographic factors that are not specific to type 1 diabetes with clinical factors specific to type 1 diabetes, this analysis was designed to inform broad interventions in the future via the identification of subgroups of patients in the first year after type 1 diabetes diagnosis who are at a higher risk for adverse longitudinal adiposity trajectories.

CONCLUSIONS

There are sex-specific changes in adiposity that occur over adolescence and into adulthood among youth with type 1 diabetes. Lower socioeconomic status appears to be associated with excess adiposity throughout adolescence in females with type 1 diabetes, independent of clinical or metabolic factors associated with weight gain. The independent contribution of socioeconomic status in males is less clear. There are likely financial or as well as specific aspects of type 1 diabetes and its clinical care to weight control in type 1 diabetes; future interventions may help to target and address health inequity to aid young individuals with type 1 diabetes maintain healthy body fat levels throughout adolescence and into adulthood.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.
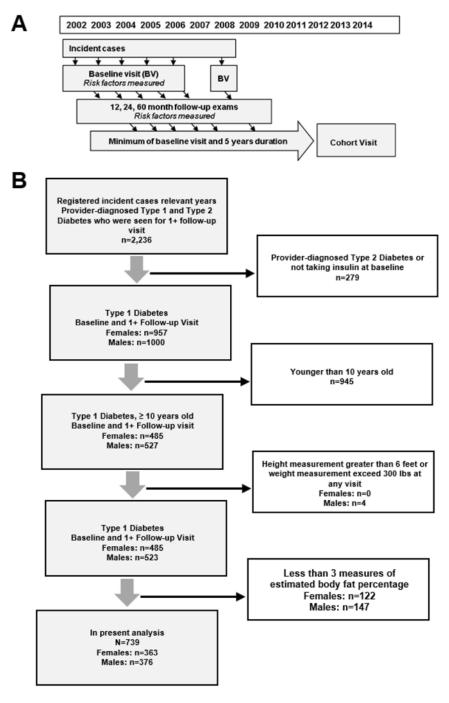
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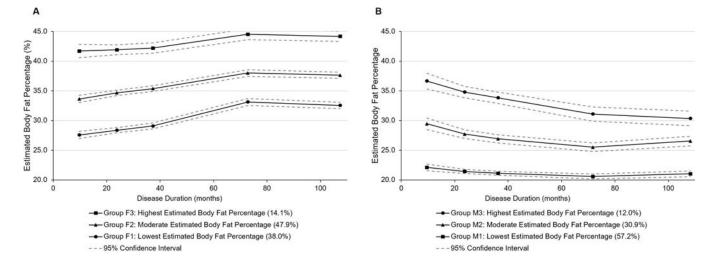
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Figure 1: Recruitment/Inclusion Criteria.
Panel A: Study design of the SEARCH Cohort Study. *Of note, the 06 and 08 incident years were not invited for the 12, 24, 60-month follow-ups, only the Cohort visit.* Panel B: Flow chart depicting participants in this report, including reasons for exclusion. The final sample included 363 females and 376 males >10 years old with type 1 diabetes.

Figure 2: Trajectories of Estimated Body Fat Percentage (eBFP) in Youth Ages 10+ with Type1 Diabetes in the SEARCH for Diabetes in Youth Study (n=363 females, n=376 males) over a mean follow-up of 107 months (with 95% confidence intervals).

Group-based trajectory modeling identified three distinct eBFP trajectories over a mean type 1 diabetes duration of 108 months in females (**2A**) and males (**2B**). All female trajectories showed gradual increases in eBFP (<5%) that plateaued by approximately 7 years of diabetes duration. Three distinct trajectories were defined by differences in baseline eBFP, including Group F1: lowest eBFP (38.0%; mean baseline eBFP: 27.8±3.0%); Group F2: moderate eBFP (47.9%; mean baseline eBFP: 33.9±3.0%), and Group F3: highest eBFP (14.1%; mean baseline eBFP: 41.7±4.1%). All male trajectories showed gradual decreases in eBFP (<5%) that plateaued by approximately 7 years of diabetes duration. Distinct trajectories were defined by differences in baseline eBFP. Including Group M1: Lowest eBFP (57.2%; mean baseline eBFP: 22.0±3.0%), Group M2: Moderate eBFP (30.9%; mean baseline eBFP), and Group M3: highest ebFP (12.0%; mean baseline eBFP: 36.1±3.7%).

Table 1A.

Baseline Demographic and Clinical Characteristics of Female SEARCH Participants with Type 1 Diabetes (Ages 10+) by Estimated Body Fat Trajectory Group (n=363)

	All Females	Group F1: Lowest eBFP	Group F2: Moderate eBFP	Group F3: Highest eBFP	
	N=362 (100.0%)	n= 138 (38.0%)	n=174 (47.9%)	n=51 (14.1%)	p-value *
Demographic Factors					
Age at Baseline, years (SD)	12.8 (2.3)	12.2 (2.3)	12.9 (2.1)	13.9 (2.8)	<0.001
Non-Hispanic White †, n (%)	253 (69.7)	105 (76.1)	121 (69.5)	27 (52.9)	0.009
Parental Education, n (%)					0.003
Less than High School	12 (3.3)	0 (0.0)	8 (4.6)	4 (7.8)	
High School Graduate	50 (13.8)	17 (12.3)	22 (12.6)	11 (21.6)	
Some College thru Assoc. Degree	131 (36.1)	43 (31.16)	66 (37.9)	22 (43.1)	
College Degree or More	170 (46.8)	78 (56.5)	78 (44.8)	14 (27.5)	
Household Structure, n (%)					0.007
Two-parent Household	236 (65.2)	100 (72.5)	113 (65.3)	23 (45.1)	
Single-parent Household	126 (34.8)	38 (27.5)	60 (34.7)	28 (58.8)	
Annual Household Income, n (%)					0.066
<$25 K	57 (15.7)	16 (11.6)	28 (16.1)	13 (25.5)	
$25–49 K	75 (20.7)	26 (18.8)	32 (18.4)	17 (33.3)	
$50–74 K	71 (19.6)	28 (20.3)	37 (21.3)	6 (11.8)	
$75+ K	136 (37.5)	58 (42.0)	66 (37.9)	12 (23.5)	
Unknown	24 (6.6)				
Health Insurance Type, n (%)					0.050
Private	283 (78.0)	117 (84.8)	132 (75.9)	34 (66.7)	
Medicaid/Medicare	66 (18.2)	18 (13.0)	33 (19.0)	15 (29.4)	
None or Other	14 (3.8)	3 (2.2)	9 (5.2)	3 (4.0)	
Clinical Factors					
Age at Diagnosis, years (SD)	11.9 (2.3)	11.4 (2.3)	12.0 (2.1)	13.2 (2.7)	<0.001
Diabetes duration, months (SD)	9.7 (6.6)	9.8 (6.4)	9.5 (6.5)	10.0 (7.6)	0.886
HbA1c, % (SD)	7.8 (1.6)	7.57 (1.3)	7.64 (1.7)	8.54 (1.8)	0.006
Insulin Regimen, n (%)					0.172
Pump	27 (7.6)	10 (7.3)	15 (8.8)	2 (4.26)	
Long + Short/Rapid Insulin, 3+ Times/Day	203 (57.2)	82 (59.9)	100 (58.5)	21 (44.7)	
Other ‡	125 (35.2)	45 (32.9)	56 (32.8)	24 (51.1)	
Insulin Dose, units per Kg (SD)	0.69 (0.34)	0.67 (0.31)	0.78 (0.77)	0.61 (0.32)	0.093
Blood Glucose Monitoring, n (%)					0.230
<1 time/day	6 (1.7)	2 (1.5)	2 (1.2)	2 (4.0)	
1–3 times/day	55 (15.5)	21 (15.6)	23 (13.3)	12 (24.0)	

	All Females	Group F1: Lowest eBFP	Group F2: Moderate eBFP	Group F3: Highest eBFP	
4+ times/day	295 (82.9)	111 (82.8)	148 (85.6)	36 (72.0)	

*
P-value estimates based on use of generalized linear models, Chi-Square, Fischer's Exact or Kruskal-Wallis Tests, as appropriate.

†
Self-reported race and ethnicity were collected using 2000 U.S. Census questions. Nonwhite includes Non-Hispanic Black, Hispanic, or other including Asian/Pacific Islander, Native American, other, or unknown.

‡
Incudes 2+ Times/Day OR Any Insulin Combination (excluding Long), 3+ Times/Day OR Any Insulin(s) taken 1x/Day, or any Insulin combination (excluding Long) 2+/Day

Table 1B.

Baseline Demographic and Clinical Characteristics of Male SEARCH Participants with Type 1 Diabetes (Ages 10+) by Estimated Body Fat Trajectory Group (n=376)

	All Males	Group M1: Lowest eBFP	Group M2: Moderate eBFP	Group M3: Highest eBFP	
	N=376 (100.0%)	n= 215 (57.2%)	n=116 (30.9%)	n=45 (12.0%)	p-value[*]
Demographic Factors					
Age at Baseline, years (SD)	13.2 (2.4)	13.7 (2.4)	12.8 (2.2)	11.9 (1.8)	<0.001
Non-Hispanic White[†], n (%)	310 (82.5)	180 (83.7)	99 (85.3)	31 (68.9)	0.036
Parental Education, n (%)					0.066
Less than High School	12 (3.2)	5 (2.4)	3 (2.6)	4 (8.9)	
High School Graduate	54 (14.6)	29 (13.7)	15 (13.0)	10 (22.2)	
Some College thru Assoc. Degree	120 (32.4)	62 (29.4)	45 (39.1)	13 (28.9)	
College Degree or More	120 (32.4)	62 (29.4)	45 (39.1)	12 (28.9)	
Household Structure, n (%)					0.807
Two-parent Household	255 (68.6)	146 (68.9)	79 (68.7)	30 (66.7)	
Single-parent Household	117 (31.4)	66 (31.1)	36 (31.3)	15 (33.3)	
Annual Household Income, n (%)					0.015
<$25 K	37 (10.0)	21 (10.0)	9 (7.8)	7 (15.6)	
$25–49 K	67 (18.1)	31 (14.8)	27 (23.5)	9 (20.0)	
$50–74 K	91 (24.6)	42 (20.0)	33 (28.7)	16 (35.6)	
$75+ K	151 (40.8)	102 (48.6)	37 (32.2)	12 (26.7)	
Unknown					
Health Insurance Type, n (%)					0.189
Private	315 (85.4)	185 (88.1)	94 (82.5)	36 (80.0)	
Medicaid/Medicare	42 (11.4)	18 (8.6)	16 (14.0)	8 (17.8)	
None or Other	12 (3.2)	7 (3.3)	4 (3.5)	1 (2.2)	
Clinical Factors					
Age at Diagnosis, years (SD)	12.3 (2.4)	12.8 (2.5)	12.0 (2.3)	11.1 (1.8)	<0.001
Diabetes duration, months (SD)	9.5 (6.4)	10.0 (6.5)	9.1 (5.9)	8.6 (6.9)	0.254
HbA1c, % (SD)	7.5 (1.6)	7.6 (1.8)	7.5 (1.4)	7.6 (1.4)	0.843
Insulin Regimen, n (%)					0.008
Pump	36 (9.8)	20 (9.5)	13 (11.8)	3 (6.7)	
Long + Short/Rapid Insulin, 3+ Times/Day	203 (55.5)	102 (48.3)	70 (63.6)	31 (68.9)	
Other[‡]	127 (34.7)	89 (42.2)	27 (24.6)	11 (24.4)	
Insulin Dose, units per Kg (SD)	0.65 (0.34)	0.63 (0.33)	0.67 (0.34)	0.74 (0.35)	0.098
Blood Glucose Monitoring, n (%)					0.412
<1 time/day	4 (1.1)	1 (0.5)	3 (2.7)	0 (0.0)	

	All Males	Group M1: Lowest eBFP	Group M2: Moderate eBFP	Group M3: Highest eBFP	
	N=376 (100.0%)	n= 215 (57.2%)	n=116 (30.9%)	n=45 (12.0%)	p-value[*]
1–3 times/day	67 (18.3)	38 (18.1)	20 (17.7)	9 (20.9)	
4+ times/day	295 (80.6)	171 (81.4)	90 (79.7)	34 (79.1)	

[*] P-value estimates based on use of generalized linear models, Chi-Square, Fischer's Exact or Kruskal-Wallis Tests, as appropriate.

[†] Self-reported race and ethnicity were collected using 2000 U.S. Census questions. Nonwhite includes Non-Hispanic Black, Hispanic, or other including Asian/Pacific Islander, Native American, other, or unknown.

[‡] Incudes 2+ Times/Day OR Any Insulin Combination (excluding Long), 3+ Times/Day OR Any Insulin(s) taken 1×2/Day, or any Insulin combination (excluding Long) 2+/Day

Table 2A.

Model Progression for Odds Ratios of Singularly Modeled Sociodemographic Predictors of Estimated Body Fat Trajectory in Females Ages 10+ with Type 1 Diabetes: SEARCH for Diabetes in Youth (n=363)

	Group F1: Lowest eBFP	Group F2: Medium eBFP	Group F3: Highest eBFP	
	n= 138 (38.0%)	n=174 (47.9%)	n= 51 (14.1%)	
	Odds Ratios (95% C.I.)	Odds Ratios (95% C.I.)	Odds Ratios (95% C.I.)	q-value[*]
Race/Ethnicity				
Model 1: Non-White race/ethnicity [†]	1.0	1.39 (0.84, 2.31)	2.83 (1.44, 5.55)	0.035
Model 2: Non-White race/ethnicity [†]	1.0	1.40 (0.74, 2.62)	1.88 (0.76, 4.62)	0.371
Household Structure				
Model 1: Single-parent household	1.0	1.42 (0.87, 2.31)	3.20, 1.65, 6.24)	0.021
Model 2: Single-parent household	1.0	1.27 (0.73, 2.19)	3.34 (1.49, 7.47)	0.036
Parental Education				
Model 1: Less than a college degree	1.0	1.60 (1.02, 2.51)	3.44 (1.70, 6.92)	0.021
Model 2: Less than a college degree	1.0	1.73 (1.04, 2.89)	3.79 (1.60, 8.99)	0.023
Health Insurance Type				
Model 1: Lack of private insurance	1.0	1.77 (0.9, 3.17)	2.79 (1.32, 5.87)	0.044
Model 2: Lack of private insurance	1.0	1.68 (0.86, 3.27)	3.74 (1.45, 9.60)	0.044
Household Income Level				
Model 1: <$75K per year	1.0	1.19 (0.75, 1.87)	2.36 (1.14, 4.90)	0.109
Model 2: <$75K per year	1.0	1.34 (0.80, 2.25)	3.13 (1.27, 7.70)	0.077

Model 3: Race/ethnicity, Household Structure, Parental Education, Health Insurance Type

Non-White race/ethnicity [†]	1.0	1.09 (0.55, 2.17)	0.80 (0.28, 2.24)	0.813
Single-parent household	1.0	1.07 (0.28, 2.24)	2.45 (1.01, 5.97)	0.154
Parental education less than college degree	1.0	1.56 (0.89, 2.72)	2.54 (1.00, 6.44)	0.130
Lack of private health insurance	1.0	1.31 (0.62, 2.75)	2.31 (0.82, 6.49)	0.333

[*] q-value reflects the overall test of difference based on the Wald test, corrected for the positive false discovery rate.[43]

[†] Self-reported race and ethnicity were collected using 2000 U.S. Census questions. White defined as non-Hispanic White. Non-White race defined as non-Hispanic Black, Hispanic, Asian//Pacific Islander, Native American, other, or unknown.

Model 1: Unadjusted model

Models 2 and 3: Adjusted for age at diagnosis, clinic site, insulin dose, insulin regime, and HbA1c at baseline.

Table 2B.

Model Progression for Odds Ratios of Singularly Modeled Sociodemographic Predictors of Estimated Body Fat Trajectory in Males Ages 10+ with Type 1 Diabetes: SEARCH for Diabetes in Youth (n=379)

	Group M1: Lowest eBFP n= 214 (56.5%)	Group M2: Medium eBFP n=116 (30.6%)	Group M3: Highest eBFP n= 49 (12.9%)	
	Odds Ratios (95% C.I.)	Odds Ratios (95% C.I.)	Odds Ratios (95% C.I.)	q-value[*]
Race/Ethnicity				
Model 1: Non-White race/ethnicity[†]	1.0	0.88 (0.47, 1.66)	2.32 (1.12, 4.81)	0.249
Model 2: Non-White race/ethnicity[†]	1.0	0.74 (0.34, 1.61)	2.19 (0.89, 5.37)	0.249
Household Structure				
Model 1: Single-parent household	1.0	0.99 (0.61, 1.61)	1.06 (0.54, 2.09)	0.884
Model 2: Single-parent household	1.0	0.93 (0.54, 1.62)	1,02 (0.47, 2.21)	0.962
Parental Education				
Model 1: Less than a college degree	1.0	1.42 (0.90, 2.23)	1.73 (0.90, 3.32)	0.320
Model 2: Less than a college degree	1.0	1.50 (0.90, 2.52)	1.39 (0.66, 2.95)	0.476
Health Insurance Type				
Model 1: Lack of private insurance	1.0	1.44 (0.79, 2.64)	1.54 (0.68, 3.52)	0.597
Model 2: Lack of private insurance	1.0	1.35 (0.67, 2.73)	1.06 (0.40, 3.80)	0.878
Household Income Level				
Model 1: <$75K per year	1.0	1,93 (1.20, 3.09)	2.48 (1.22, 5.06)	0.042
Model 2: <$75K per year	1.0	1.70 (1.01, 2.88)	1.79 (0.91, 4.01)	0.249

Model 3: Race/ethnicity, Household Structure, Parental Education, Health Insurance Type

Non-White race/ethnicity[†]	1.0	0.66 (0.30, 1.46)	2.03 (0.81, 5.12)	0.249
Single-parent household	1.0	0.83 (0.47, 1.48)	0.80 (0.35, 182)	0.884
Parental education less than college degree	1.0	1,33 (0.75, 2.34	1.11 (0.49, 2.52)	0.876
Household income level <$75K per year	1.0	1.63 (0.91, 2.91)	1.61 (0.66, 3.94)	0.420

[*] q-value reflects the overall test of difference based on the Wald test, corrected for the positive false discovery rate.[43]

[†] Self-reported race and ethnicity were collected using 2000 U.S. Census questions. White defined as non-Hispanic White. Non-White race defined as non-Hispanic Black, Hispanic, Asian//Pacific Islander, Native American, other, or unknown.

Model 1: Unadjusted for covariates

Models 2 and 3: Adjusted for age at diagnosis, clinic site, insulin dose, insulin regimen, and HbA1c at baseline.