Insulin Regimens and Clinical Outcomes in a Type 1 Diabetes Cohort

The SEARCH for Diabetes in Youth study

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OBJECTIVE—To examine the patterns and associations of insulin regimens and change in regimens with clinical outcomes in a diverse population of children with recently diagnosed type 1 diabetes.

RESEARCH DESIGN AND METHODS—The study sample consisted of youth with type 1 diabetes who completed a baseline SEARCH for Diabetes in Youth study visit after being newly diagnosed and at least one follow-up visit. Demographic, diabetes self-management, physical, and laboratory measures were collected at study visits. Insulin regimens and change in regimen compared with the initial visit were categorized as more intensive (MI), no change (NC), or less intensive (LI). We examined relationships between insulin regimens, change in regimen, and outcomes including A1C and fasting C-peptide.

RESULTS—Of the 1,606 participants with a mean follow-up of 36 months, 51.7% changed to an MI regimen, 44.7% had NC, and 3.6% changed to an LI regimen. Participants who were younger, non-Hispanic white, and from families of higher income and parental education and who had private health insurance were more likely to be in MI or NC groups. Those in MI and NC groups had lower baseline A1C ($P = 0.028$) and smaller increase in A1C over time than LI ($P < 0.01$). Younger age, continuous subcutaneous insulin pump therapy, and change to MI were associated with higher probability of achieving target A1C levels.

CONCLUSIONS—Insulin regimens were intensified over time in over half of participants but varied by sociodemographic domains. As more intensive regimens were associated with better outcomes, early intensification of management may improve outcomes in all children with diabetes. Although intensification of insulin regimen is preferred, choice of insulin regimen must be individualized based on the child and family's ability to comply with the prescribed plan.

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*A complete list of the SEARCH for Diabetes in Youth Study Group can be found in the Supplementary Data online.

The Diabetes Control and Complication Trial (DCCT) clearly established the benefits of intensive versus conventional insulin therapy in adolescents and adults with type 1 diabetes (1). Improved glycemic control, measured by lower A1C levels, reduced the risk for onset and progression of long-term diabetes microvascular and macrovascular complications (2).

Since the DCCT was conducted, significant advances in diabetes management have occurred, including newer and more physiologic insulin analogs, sophisticated blood glucose monitoring, and insulin delivery technologies such as continuous subcutaneous insulin pump therapy (CSII) and continuous glucose monitoring (CGM). Current recommendations from the American Diabetes Association (ADA) and International Society for Pediatric and Adolescent Diabetes endorse the use of intensive insulin regimens in most pediatric patients. Additionally, the ADA recommends the following age-specific A1C goals for children: <6 years of age, 7.5–8.5%; 6–12 years, ≤8.0%; 13–18 years, ≤7.5%; and >19 years, ≤7.0% (3). However, it is unclear whether intensive insulin regimens used in clinical pediatric diabetes care result in different A1C outcomes (4,5).

The SEARCH for Diabetes in Youth study has reported that insulin treatment regimens were cross-sectionally associated with sociodemographic, clinical, and metabolic characteristics among youth with type 1 diabetes (6). Sociodemographic factors were strongly associated with insulin regimen used, with participants more likely to be using intensive regimens, such as CSII, if they were of non-Hispanic white race/ethnicity and from families with higher income and higher parental education, and had private health insurance. CSII therapy was associated with lowest A1C levels in all age-groups. Higher frequency of blood glucose monitoring was also associated with a lower A1C within each treatment group. No significant differences were observed in the frequency of hypoglycemia

or emergency department visits between insulin regimen groups; however, frequency of hospitalizations was lower in participants who were on CSII therapy than other insulin regimens. Overall, adolescents had unacceptably high A1C levels, with 70% having levels >7.5% regardless of insulin regimen. While these observations yield valuable information about insulin regimens and A1C outcomes, gaps in our existing knowledge result in limited evidence-based guidelines to indicate how such regimens can be applied most optimally over time to individuals with varied resources.

There is a paucity of information about changes in insulin regimens and outcomes over time, particularly early in the clinical course of type 1 diabetes. In the DCCT, intensive therapy was associated with preserved β-cell function, which in turn was associated with improved glycemic control and decreased risk of severe hypoglycemia. In fact, current immuno-intervention trials are designed to preserve β-cell function and attempt to account for the effect of intensive therapy by ensuring that the control group as well as treatment group(s) are closely followed and managed with intensive regimens (7,8). However, there is little information regarding the role of insulin treatment regimens in preservation of β-cell function and short-term outcomes.

This report describes a cohort of participants from the SEARCH study who have been followed over time with an initial visit in the first year after diagnosis, providing an opportunity to examine whether insulin regimen intensification over time significantly impacts metabolic outcomes in youth with type 1 diabetes.

RESEARCH DESIGN AND METHODS

Overview of the SEARCH study

SEARCH is an ongoing multicenter study that conducts population-based ascertainment of newly diagnosed cases of nongestational diabetes in youth <20 years of age (9). For this study, youth with diabetes were identified in geographically defined populations in Ohio, Washington, South Carolina, and Colorado; among managed health care plan enrollees in Hawaii and California; and among Indian Health Service beneficiaries in selected American Indian populations. Cases are considered valid if diagnosed by a health care provider. For all validated cases, core demographic and diagnostic information, including date of birth, sex, date of diagnosis, and clinical diabetes type, was obtained from medical records, usually as part of the case validation process. The clinical diabetes type assigned by the health care professional was obtained from medical records or physician reports and categorized as follows: type 1 (combining type 1, type 1a, and type 1b), type 2, and other types (including hybrid type, maturity onset diabetes of the young, type unknown by the reporting source, type designated as other, and missing type). Self-reported race and ethnicity information was collected through an initial survey using the 2000 U.S. Census questions (10).

Youth with nonsecondary diabetes who replied to the initial survey were invited to a baseline study visit while metabolically stable (no episode of diabetic ketoacidosis during the previous month). On average, visits occurred 10 months after diabetes diagnosis. Participants who were diagnosed in 2002–2005 were also invited back for follow-up study visits at ~12 and 24 months after the baseline visit. Written informed consent and assent were obtained according to guidelines established by the local institutional review boards.

Study population

For this report, participants were included if they had type 1 diabetes, were taking insulin, and had a baseline and at least one follow-up study visit. Participants were excluded if key measures, including insulin treatment regimen, A1C, and fasting C-peptide (FCP), were missing. The final study sample included 1,606 youth with type 1 diabetes who had a baseline and at least 1 follow-up visit; 76% of those had at least two follow-up visits.

Data collection

After an 8-h, overnight fast, participants attended a study visit. Participants were instructed not to take diabetes medications the morning of the visit except for basal insulin administered by a continuous insulin infusion pump. Physical examinations at the study visits were conducted according to standardized protocols by trained and certified staff members. Height and weight were measured to the nearest 0.5 cm and 0.1 kg. BMI was calculated as weight in kilograms divided by the square of height in meters and converted to BMI *z* score using the standard Centers for Disease Control and Prevention approach (11). At the visits, information was collected on demographics, duration of diabetes, household income, highest level of education of either parent/guardian, health insurance status, and type of provider delivering diabetes care (e.g., pediatric endocrinologist, adult endocrinologist, family practitioner). Blood was drawn to measure A1C and FCP.

A1C was measured by a dedicated ion-exchange high-performance liquid chromatography instrument (Tosoh Bioscience, San Francisco, CA). FCP was measured by a two-site immunoenzymetric assay (Tosoh Bioscience). The assay sensitivity is 0.05 ng/mL.

Self-reported information obtained at the time of the study visit used for these analyses included history of insulin use, number of daily injections, types of insulin, mode of insulin delivery (e.g., insulin syringes or insulin pen devices, CSII), and frequency of self–blood glucose monitoring (SBGM). Additional information was collected by self-report related to acute clinical complications occurring within the 6 months prior to the study visit, including episodes of severe hypoglycemia (defined as "very low blood sugar that required you to get help"), hospital admission, or emergency department visits. The same data were also collected at follow-up visits.

Treatment regimens

Insulin regimens were classified into five categories, with category 1 considered most intensive and category 5 least intensive, as follows: *1*) basal-bolus with CSII; *2*) basal-bolus with glargine or detemir plus rapid-acting insulin (insulin lispro, insulin aspart, or insulin glulisine); *3*) multiple daily injections (MDIs) (three or more injections) with glargine or detemir insulin plus NPH insulin plus regular or rapid-acting insulin; *4*) MDI (three or more injections) with any insulin types excluding basal insulin (glargine or detemir); and *5*) one to two injections per day, excluding insulin glargine or detemir. These categories represented basal-bolus regimens (regimens 1 and 2), modified basal-bolus regimens (regimen 3), MDIs (regimen 4), or what had been considered standard therapy at the initiation of the DCCT (regimen 5).

Change groups

Participants' insulin regimens were categorized based on the insulin regimen used at baseline compared with their regimen at their most recent follow-up visit. Those who changed to a more intensive (MI) regimen included those moving from a higher to lower category, e.g., from regimen 4, MDIs without basal insulin, to regimen 1, CSII. The no change (NC) group is the group who stayed in the same category. The less intensive (LI) moved from a lower to higher category, e.g., moving from regimen 2, basal-bolus, to regimen 5, one to two injections/day without basal insulin.

Table 1—*Demographics of participants by insulin regimen change group*

	MI	NC	LI	*P***
n	830	718	58	
Age at baseline visit, years, mean (SD)	9.4 (4.0)	10.3 (4.6)	12.1 (4.3)	<0.0001
Age at diagnosis, years, mean (SD)	8.2 (4.0)	9.0 (4.6)	10.6 (4.2)	<0.0001
Duration of diabetes at baseline, months, mean (SD)	8.7 (5.8)	10.6 (6.3)	13.2 (7.2)	<0.0001
Duration of diabetes at follow-up 1, months, mean (SD)	22.5 (6.9)	24.3 (6.9)	27.1 (8.8)	<0.0001
Duration of diabetes at follow-up 2, months, mean (SD)	34.8 (6.8)	36.2 (7.4)	38.9 (7.7)	<0.0001
Sex				
Male	418 (49.7)	392 (/46.6)	31 (3.7)	0.2471
Female	412 (53.9)	326 (42.6)	27 (3.5)	
Race				
Black	49 (35.5)	82 (59.4)	7 (5.1)	0.0003
Hispanic	83 (47.7)	84 (48.3)	7 (4.0)	
Other	44 (43.6)	50 (49.5)	7 (6.9)	
White	654 (54.8)	502 (42.1)	37 (3.1)	
Household income (USD)				
<25,000	82 (37.3)	126 (57.3)	12 (5.5)	<0.0001
25,000–49,000	162 (47.0)	167 (48.4)	16 (4.6)	
50,000–74,000	165 (50.9)	146 (45.1)	13 (4.0)	
≥75,000	364 (59.7)	236 (38.7)	10 (1.6)	
DK/refused	57 (54.3)	41 (39.1)	7 (6.7)	
Maximum parental education				
Less than high school graduate	23 (34.3)	37 (55.2)	7 (10.5)	<0.0001
High school graduate	98 (42.2)	122 (52.6)	12 (5.2)	
Some college through associates degree	268 (48.4)	266 (48.0)	20 (3.6)	
Bachelor's degree or more	441 (58.6)	292 (38.8)	19 (2.5)	
Health insurance				
Private	694 (54.6)	531 (41.8)	47 (3.7)	<0.0001
Medicaid/Medicare	111 (39.0)	163 (57.2)	11 (3.9)	
Other	16 (76.2)	5 (23.8)	0 (0.0)	
None	7 (30.4)	16 (69.6)	0 (0.0)	
Type of diabetes care provider				
Pediatric endocrinologist	671 (52.2)	574 (44.6)	41 (3.2)	0.0153
Adult endocrinologist	2 (14.3)	10 (71.4)	2 (14.3)	
Generalist	14 (37.8)	20 (54.1)	3 (8.1)	
Nurse practitioner/physician's assistant	133 (54.3)	102 (41.6)	10 (4.1)	
Other	9 (39.1)	12 (52.2)	2 (8.7)	
Insulin regimen at baseline*				
1	0 (0.0)	108 (83.7)	21 (16.3)	<0.0001
2	197 (38.0)	299 (57.7)	22 (4.3)	
3	53 (44.5)	58 (48.7)	8 (6.7)	
4	155 (66.2)	72 (30.8)	7 (3.0)	
5	425 (70.1)	181 (29.9)	0 (0.0)	
Center				
A	166 (52.0)	140 (43.9)	13 (4.1)	0.0005
B	147 (51.9)	125 (44.2)	11 (3.9)	
C	267 (56.7)	194 (41.2)	10 (2.1)	
D	60 (40.3)	79 (53.0)	10 (6.7)	
E	174 (52.9)	146 (44.4)	9 (2.7)	
F	16 (29.1)	34 (61.8)	5 (9.1)	

Data are *n* (%) unless otherwise indicated. *N* = 1,606. ***P* values are from ANOVA for continuous variables and χ^2 tests of association for categorical variables. *1, pump; 2, MDI: glargine/rapid; 3, MDI: glargine/rapid plus other; 4, MDI: no glargine; and 5, one to two injections/no glargine. DK, don't know.

Statistical analyses

Statistical analyses were conducted using SAS (version 9.2; SAS Institute, Cary, NC). Outcome variables with skewed distribution were log transformed. Demographic measures were summarized by their mean (SD) or *n* (%) for categorical measures. Comparisons of means and categorical frequencies across the three insulin regimen change groups were tested using ANOVA or the χ^2 statistic. The number of participants, mean (SE) A1C at baseline, and mean A1C at last follow-up exam are presented by the insulin regimen group at baseline compared with the insulin regimen group at last follow-up. The means (SE) of the outcome measures are presented by change group and visit. The adjusted means (least square means) (SE) were estimated using repeated-measures ANCOVA. The covariates included the measure of the outcome at baseline and age, race/ethnicity, research site, household income, health insurance status, and parental education. Contrasts were formed to make pairwise comparisons between the change groups at each of the follow-up visits. The adjusted means (SE) of the outcomes were estimated for each most recent insulin regimen and visit adjusting for the covariates listed above. The equality of the adjusted means across the five insulin regimens was tested using ANCOVA musing contrasts to test the equality separately at each of the visits. The means (SD) of A1C are given by change group by visit by whether the subject was testing blood glucose four or more times a day. For each change group by visit, the means of A1C by whether they test four or more times per day were compared and tested using a two-sample *t* test. The adjusted means (SE) were estimated using ANCOVA, adjusting for the demographic factors listed above as covariates, and the groups were compared for each change group by visit. The percent of participants that achieved the ADA target A1C at last follow-up was compared by the χ^2 test separately for three age-groups.

RESULTS—Demographic and clinical characteristics of the participants, by insulin regimen change group, are shown in Table 1. Between baseline and most recent follow-up visit, just over half of the participants (51.7%) changed to an MI regimen, 44.7% had no change, and 3.6% changed to an LI regimen. Most (76%) of the participants had two follow-up visits; only 2% of these participants had an interval change at the first follow-up that was not consistent with the direction of change at the most recent follow-up. Age, diabetes duration, sociodemographics, and type of provider for diabetes care differed significantly between change groups (Table 1). The MI group was younger than NC and LI ($P < 0.0001$), with shorter duration of diabetes at each visit ($P < 0.0001$); was more likely to be NHW ($P = 0.0003$); and had a higher household income ($P < 0.0001$) and a higher parental education level ($P < 0.0001$). Those in the MI group were more likely to have private health insurance and to be seen by a pediatric endocrinologist than those in the LI group ($P < 0.0001$ and $P = 0.015$, respectively).

There was a significant intensification of insulin therapy over the duration of the study in this large diverse population. At baseline, the MI group had a lower proportion of participants on more intensive management and a higher proportion on the least intensive regimen than either the NC or the LI groups. Of the participants who were on regimen 4 or 5 at the initial visit, 63.3% were on more intense regimens at the most recent follow-up visit, with 25.6% on CSII therapy at follow-up. Of note, in the NC group 108 (15%) were on CSII (insulin regimen category 1) at their baseline visit and 407 (56%) were in either insulin regimen category 1 or 2 at baseline, indicating an already intensive regimen at baseline.

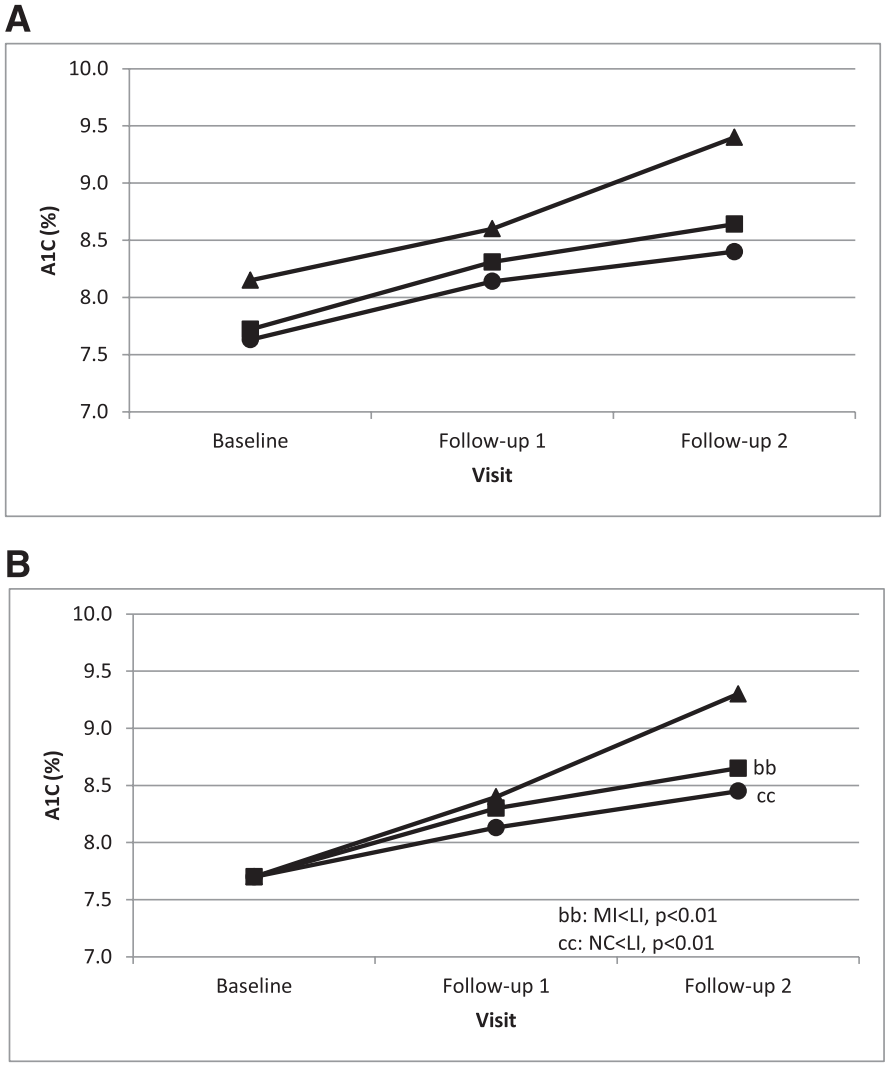

Figure 1—A: *Visit, mean A1C during follow-up by regimen change group, unadjusted.* ●, *MI;* ■, *NC;* ▲, *LI.* B: *Visit, A1C during follow-up adjusted for baseline values of A1C, FCP, and demographics by regimen change group. Demographics include race, sex, research site, age, duration of diabetes, maximum parental education, family income, and health insurance.* ●, *MI;* ■, *NC;* ▲, *LI; bb, MI < LI,* P *< 0.01; cc, NC < LI,* P *< 0.01.*

Treatment change group, A1C, and achieving ADA A1C targets

At baseline, the LI group had a higher A1C than the MI and NC groups (P = 0.028) (Fig. 1*A*). While A1C increased significantly over time in all groups, after adjustment for repeated measures, baseline A1C, and demographics, the MI had a lower A1C over time than the NC at both the 1-year and 2-year visits ($P < 0.05$) (Supplementary Table 1). Both MI and NC showed a smaller increase in A1C compared with the LI group (Fig. 1*B*). Children <6 years old were more likely to achieve the ADA target level for A1C representing good glycemic control, and those >12 years old were least likely to do so regardless of change group (Fig. 2). Of note, the majority of children >6 years of age did not achieve the ADA target for A1C regardless of change group. CSII therapy shows a significantly lower A1C at each follow-up time point ($P < 0.001$), adjusted for demographics, even though CSII users had lowest FCP over time ($P < 0.001$) (Supplementary Table 2). Overall younger age, CSII therapy, and change to MI were associated with higher probability of meeting optimal target AIC levels before and after adjustment for demographics.

A1C and self-glucose monitoring

The majority (86–91%) of participants reported testing blood glucose at least four times daily. At all visits and in all treatment regimens, those testing at least four times/day had lower mean A1C levels (Supplementary Table 3). After adjustment for baseline age, duration of diabetes, sex, household income, parental education, and type of health insurance, this trend continued. In almost all comparisons at the two follow-up times, the mean level of A1C was significantly lower in the case of testing four or more times per day unadjusted or adjusted for demographic factors.

FCP

Mean FCP was 0.69 ng/mL at baseline with no significant differences among NC, MI, and LI groups (Fig. 3*A*). In all groups, FCP declined ($P < 0.0001$) over time. After adjustment for baseline FCP and demographics, FCP was significantly higher in LI and NC versus MI ($P < 0.01$) (Fig. 3*B*).

BMI z score was not significantly different between change groups at any time point (Supplementary Table 2). Similarly, BMI was not different by insulin regimen and did not increase over time more dramatically on any particular regimen (Supplementary Table 3).

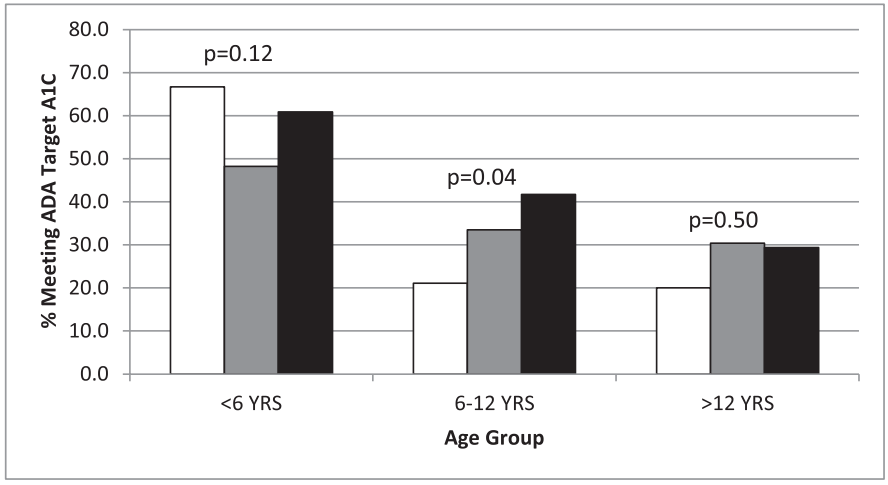

Figure 2—*Age-group, percent meeting ADA target A1C at follow-up by regimen change group, and age-group, unadjusted. Open bar, LI; gray bar, NC; dark bar, MI.*

Hypoglycemic events were not different by change group at any time point (Supplementary Table 2). Participants in the MI group had fewer emergency department visits than those in LI at the follow-up visit 2 ($P < 0.05$), but there was no difference in frequency of hospitalizations by change group.

CONCLUSIONS—To our knowledge, this is the first report of change in insulin regimen over time in a contemporary cohort of youth with type 1 diabetes. At enrollment or over the course of this study, a majority of participants either used or moved to an intensified insulin therapy regimen. By a mean diabetes duration of ~36 months, almost three-quarters of participants were using basal-bolus therapy as either CSII or MDIs. Sociodemographic factors were highly associated with treatment regimen and the likelihood of moving to an MI regimen. Specifically, higher parental education, higher family income, and having private health insurance were all positively associated with an intensification of insulin regimen over time. These data are consistent with cross-sectional studies reporting an association of sociodemographics with treatment regimen.

Participants on intensified insulin regimens had lower A1C levels over time. This difference remained significant when adjusted for baseline A1C. After adjusting for sociodemographic variables (age and race/ethnicity), the difference in A1C between groups was less striking. However, the LI group still had persistently higher A1C than MI or NC groups. Our results are similar to those observed in retrospective study from a single academic pediatric practice, where intensive insulin regimens started at diagnosis were associated with improved glycemic control in patients on private insurance and were not associated with worse glycemic control in those on the public health plan, Medicaid (12).

Important differences between these studies are that the results we present are from a longitudinal study of participants from six different research sites, each including a mix of academic versus nonacademic practices. Also, a focus of our study was to assess whether change in regimen was associated with improved outcomes, as was the case. Furthermore, SEARCH participants using CSII at their final visit had lower A1C than those using other treatment regimens regardless of baseline treatment regimen.

An integral part of intensive self-management of diabetes is frequent glucose monitoring. The frequency of four or more blood glucose tests/day (87.3%) at baseline indicates that frequent glucose monitoring is endorsed by diverse practice models across the U.S. and also documents the intensity of care recommended at diagnosis. Furthermore, the 82% overall report of this frequency of glucose monitoring at the follow-up visit confirms families' understanding that continuing glucose monitoring is an important component of diabetes care. Importantly, over time, glucose monitoring at a rate of four or more tests/day was associated with lower A1C within all change regimens, which validates the essential nature of frequent glucose testing to guide more optimal diabetes care. This

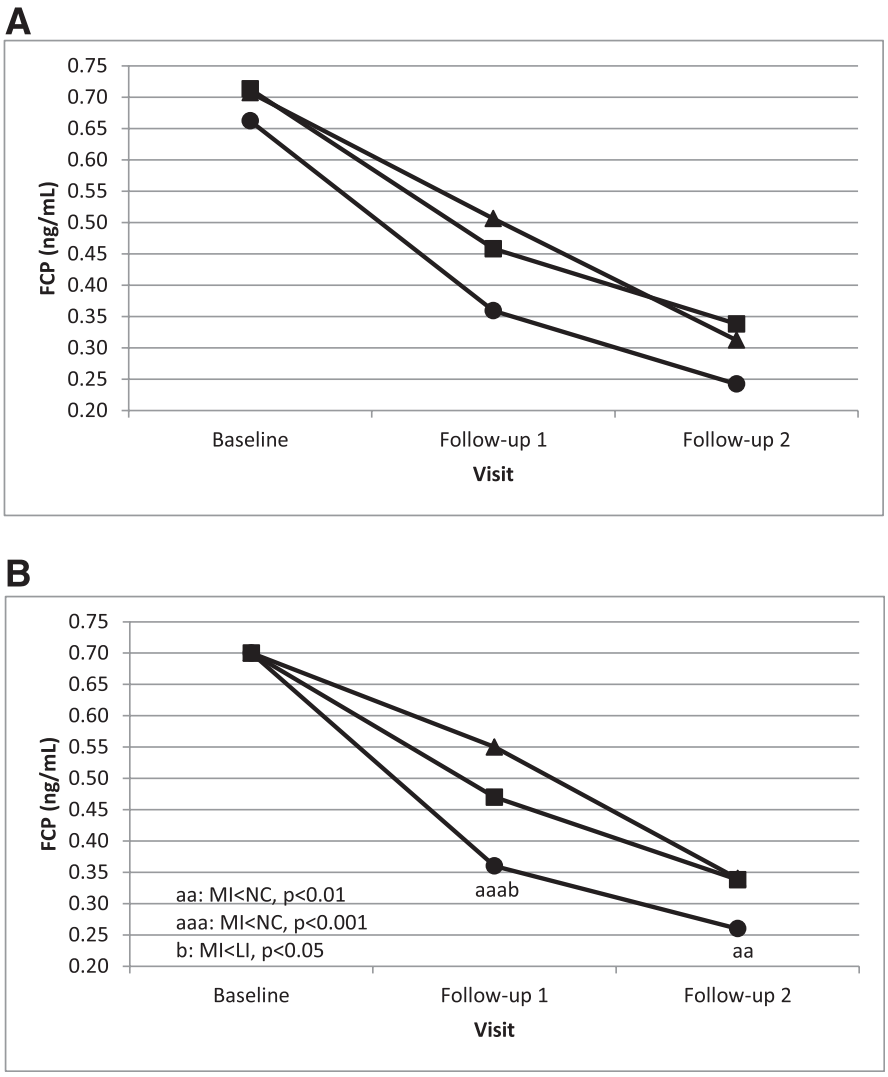

Figure 3—A: *Visit, mean FCP during follow-up visits by regimen change group (unadjusted).* ●, *MI;* ■, *NC;* ▲, *LI.* B: *Visit, mean FCP during follow-up by regimen change group adjusted for baseline FCP and demographics. (Demographics include race, sex, clinic, age, duration of diabetes, maximum parental education, income, and insurance.)* ●, *MI;* ■, *NC;* ▲, *LI; aa, MI* < *NC,* P < *0.01; aaa, MI* < *NC,* P < *0.001; b, MI* < *LI,* P < *0.05.*

association of more frequent glucose monitoring for children on various insulin regimens with lower A1C has been observed in cross-sectional studies, including SEARCH (6,13,14). Additionally, the proportion of participants with less frequent monitoring varied by change group, at baseline and follow-up, as shown in Supplementary Table 4; at visit 2, 45% of those in the LI group were monitoring between zero and three times/day compared with 23.8% in the NC group and 13.5% in the MI group. This observation also strongly suggests that adherence to self-management tasks was poorer in the LI group and likely influenced the choice of insulin treatment regimen.

A decline in FCP levels occurred in all insulin regimen groups. Intensified insulin therapy did not appear to provide protection against the temporal decline in FCP. In fact, those in the LI group had a higher FCP than the MI and NC groups with and without adjustments. This may be due to the fact that providers may recommend less intensive insulin regimens to youth with more preserved β-cell function. Also, the LI group was older, which may explain both their higher mean FCP at baseline and the more gradual rate of decline. Given the descriptive nature of the study, it is not possible to determine factors contributing to treatment recommendations. However, intensification of insulin therapy over time was associated with better glycemic control, which was not attributable to preserved C-peptide. Because FCP was lower in more intense regimens, we speculate that these participants may have experienced greater glucose variability, more significant hyperglycemia, and/or higher A1C at clinical visits, prompting their care providers to intensify the treatment regimen. On the other hand, it is worth pointing out that although the LI group had higher FCP levels, this did not result in better glycemic control, and some of these individuals may benefit from insulin treatment intensification.

These data support an approach to diabetes management that includes an intensification of insulin regimen over time. The fact that the more intensive and no change groups were not significantly different in a fully adjusted model reflects, in part, the high frequency of starting on rather intensive therapies, e.g., basal-bolus in the NC group. The fact that A1C was most strongly associated with insulin regimen at follow-up also speaks to the importance of intensification over time. The data also emphasize the importance of identifying better therapies for all youth with diabetes. Also, as consistently reported in cross-sectional studies, there is a need for additional work in identifying the barriers to care in adolescents, given that only a minority is achieving acceptable glycemic control. These data do provide U.S. benchmarks from a large, diverse population for A1C values over time as well as frequency of hypoglycemia, emergency department visits, and hospitalizations in children with type 1 diabetes cared for outside of a randomized, controlled trial.

Limitations to this report include the fact that these findings may not be generalizable to all children with diabetes. While there was much effort to recruit and encourage visits for all eligible participants, participation in research studies is elective. Older youth are less likely to participate (15). In our study population, those in the LI group were older and had a longer duration of diabetes. While longer duration is associated with a higher A1C and lower FCP, duration was included in our regression model to account for this important variable; therefore, the findings in the LI group are likely to reflect the larger SEARCH population. At this time, we are unable to comment on factors contributing to decisions related to diabetes management in the SEARCH cohort, including insulin regimen and frequency of glucose monitoring. Subsequent follow-up of SEARCH participants is designed to address some of these factors, including additional measures of barriers to more optimal glycemia such as

fear of hypoglycemia and out-of-pocket expenses for diabetes supplies.

The strengths of this study include its large, racially/ethnically and socioeconomically diverse composition. This is an observational study from multiple centers and encompasses participants whose care is delivered in a variety of practice models ranging from academic multidisciplinary specialty clinics to public health centers. Also, the longitudinal nature of the study allowed for building on SEARCH's previous cross-sectional reports, including the key finding that intensification of insulin regimens over time was associated with better glycemic control.

In conclusion, for the majority of youth in this study, insulin regimen intensified over time, and more intensive regimens were associated with lower A1C. However, health care inequities were observed in that minority youth and those from families with lower income and less parental education were less likely to have their insulin regimens intensified. Frequent glucose monitoring was highly associated with better glycemic control within all treatment regimens, reflecting that this is an essential component to optimal diabetes care. More intensive management was not associated with a slower decline in C-peptide levels. Because intensive diabetes care is generally associated with higher supply costs, it may be subject to scrutiny by payer systems. Taking together the better outcomes but sociodemographic disparities in intensification of insulin regimens, there is a dire need to develop strategies to improve care for all children with diabetes.

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C.P. designed the study, obtained funding, researched the data, and wrote the manuscript. A.B. designed the study, obtained funding, contributed to discussion, and edited the manuscript. A.A. and T.M. analyzed data and edited the manuscript. L.D. and D.D. designed the study, obtained funding, contributed to discussion, and edited the manuscript. G.I., B.L., and S.M. contributed to discussion and edited the manuscript. E.M.-D. designed the study, obtained funding, contributed to discussion, and edited the manuscript. K.R. contributed to discussion and edited the manuscript. G.J.K. designed the study, obtained funding, researched the data, and wrote the manuscript. C.P. and G.J.K. are the guarantors of this work and, as such, had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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