Diabetes in Native Youth: The SEARCH for Diabetes in Youth Study

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Dana Dabelea:

I'm Dana Dabelea. I am trained as a diabetologist and diabetes epidemiologist with a medical degree from Romania, and a PhD in Epidemiology in this country. I am now a Professor of Epidemiology and Pediatrics at the University of Colorado, Denver, and also serve as Associate Dean for Faculty Affairs at the Colorado School of Public Health. I have been involved with the SEARCH study since 2001, and for the past 10 years, I have been the Co-chair of the study together with a very dear colleague and friend from the University of North Carolina, Dr. Beth Mayer-Davis.

And I'm just going to continue to present, right?

Jan Frederick:

Yes, go ahead.

Dana Dabelea:

Okay. So what you have here is just a brief outline of the presentation. I will talk a little bit about a rationale for SEARCH, the study design, the contributions that the study has made to the field of pediatric diabetes, some plans for the future, and how SEARCH is informing interventions. I'm going to end with a pilot intervention study that we're currently conducting in Indian Country that was inspired by SEARCH.

So way back in 2000 when the study was funded, we really were starting to see an increase in type 2 diabetes in children in several populations in the United States especially minority populations. Actually, I was working with the Pima Indians, in the Pima Indian study during that period, and we were reporting for the first time in the medical literature an epidemic of type 2 diabetes in youth that really was one of the strongest motivators for the SEARCH study. At the same time, worldwide, there was an increase in type 1 diabetes incidence with mostly data from Europe but across the entire world, with limited data from the United States because there were no nationwide registries to track trends in incidence of type 1 diabetes at that time.

So these were the two main motivators for SEARCH. But at the same time, with the epidemic of obesity, we were starting to see reports of atypical diabetes with mixed phenotypes labeled hybrid diabetes, double diabetes, and diabetes 1.5, LADA in adults. So we really wanted to see if this is a new form of diabetes or something that is really due to the obesity epidemic. So, several funding agencies have come together and funded the SEARCH study way back in 2000, primarily the Centers for Disease Control and Prevention in Atlanta and the NIDDK.

The SEARCH study, as you can see here, now has five clinical sites. In the beginning, it had a sixth one that we lost along the way. But right now, there are five clinical sites located as you can see on this map. I'm going to start with my site, the University of Colorado Denver. Here, I'm trying to use the

arrow but I can't. The University of Colorado Denver is covering the entire state of Colorado and has been working with several Native American tribes in New Mexico and in Arizona, primarily with the Navajo Nation at this point in time.

The other sites are located in Washington; Seattle Children's Hospital is leading that effort in Seattle, Cincinnati Children's Hospital covering Ohio, and the state of South Carolina coordinated now by the University of North Carolina at Chapel Hill. Then we have what we call a membership-based site at Kaiser Permanente in Southern California. The other four sites that I have described are geographic-based sites. Kaiser is obviously a membership-based site. We have a central coordinating center at Wake Forest University in North Carolina, and a central lab in Seattle, Washington.

So the next slide shows you the design of SEARCH. It's a busy slide but I think it describes pretty well how we operate. So SEARCH is a mixture of two studies actually. A mixture of what we call a registry study and a cohort study. So the registry study really aims to identify, to ascertain all kids with diabetes, all kids age less than 20, who have diabetes of any type residing in the locations I've just described. So SEARCH is designed to do that and identify all these children with diabetes, building local site registries, and then registering these cases in a de-identified way with the central registry located at Wake Forest University.

Again, I'm saying this several times, we have to identify all kids with diabetes because we are a registry study and we want to track prevalence and incidence and trends. Then once these kids are identified, we try to collect data to inform what we call the cohort study. So we invite them to participate in voluntary data collection, and we start with a baseline visit and continue with several follow-up visits at 12, 24, 36 months from diagnosis, and another visit after five years from diagnosis in what we call the cohort visit.

At each of these visits, we conduct a brief physical exam measuring height and weight, and waist circumference. We draw blood to measure several things that are important like hemoglobin A1c, lipids, inflammatory markers. We store blood and we store DNA. We collect urine to measure microalbuminuria and creatinine in the urine. We store urine, as well, and we administer questionnaires.

So what are the populations under surveillance? Obviously, they are the populations in the locations that were shown on the map. This is our denominator. This is the population of youth at risk for diabetes that we are surveying. For California, about 790,000 kids annually. For Colorado, which is the largest site, we have about 1.4 million children. The Native American sites are listed here; Ohio, South Carolina, Washington, for a total of almost five million children age less than 20 at risk for diabetes throughout these locations that we survey every year to ascertain patients for diabetes.

How do we do that, how do we identify kids with diabetes in these populations? This slide shows that for each of our sites there is a combination of pediatric endocrinology practices and other case sources, including hospitals, other pediatricians, adult endocrinologists, certified diabetes educators, community health centers. And for the Navajo Nation which I have listed here under the Colorado site, we work with the eight Indian Health Service Units located there.

So if we were doing a good job, then this is what we are identifying. We are identifying youth with physician-diagnosed diabetes that were aged less than 20 in 2001 and in 2009, the two years in which we estimated prevalence of diabetes, or aged less than 20 at diagnosis in year 2002 onwards for our estimates of incidence which we are currently continuing to do since 2002.

These youth are residents of the population defined by those geographic locations or members of the health plans that I have described, Kaiser Permanente, or for our work with the Navajo Nation, users of the Indian Health Service system. They should not be active-duty military, not institutionalized, and we

are not ascertaining gestational diabetes at this time. However, if somebody has been diagnosed with diabetes outside of their pregnancy, they are eligible to participate.

So I'm going to go over a few of the major contributions of SEARCH to the field of pediatric diabetes, and I'm going to start with the burden of diabetes. As I said in 2000, we had very little or limited data in the U.S. about prevalence or incidence of type 1 or type 2 diabetes and for sure not rates by race ethnicity. So as soon as we started, we were able to determine or estimate incidence of type 1 diabetes, and what you're going to see here is incidence of type 1 diabetes in 2002-2003 by age and race ethnicity.

So you're seeing here the incidence per 100,000 per year of type 1 diabetes by age group and by racial ethnic group. As you can see, the incidence of type 1 peaks around puberty, 10 to 14, and a little earlier, 5 to 9 year-old age groups. It is highest in non-Hispanic white children, perhaps peaking, at that time, more than 30 per 100,000 per year in kids 10 to 14. Then declining a little bit or being a little lower among the – African Americans in red, Hispanics in orange, Asian-Pacific Islanders in blue, and American Indians in gray. But there is type 1 diabetes in all racial ethnic groups.

This next slide shows the incidence of type 2 diabetes over the same period, again by age and race ethnicity. And notice, I am not showing the younger age groups because at least at that time there was virtually no type 2, or very little type 2 diabetes at ages younger than 10. But what you can see here is that there is type 2 diabetes in all racial ethnics groups, and the older the kids are, the more type 2 diabetes there is, and that the leading group is American Indians with almost 50 per 100,000 per year in American Indians aged 15 to 19, which is the highest incidence of any form of diabetes in any racial ethnic group in children.

More recently, this paper just came out in JAMA this year. We were able to put together our prevalence data from 2001 and 2009, and estimate, determine whether there were trends or changes in the prevalence of type 1 and type 2 diabetes over time. And so this shows the trends in type 1 diabetes prevalence between 2001 and 2009 over only eight years, an eight-year period, by age, sex, and race ethnicity. And perhaps not unexpectedly, but daunting, there was an overall increase of 21% in the prevalence of type 1 diabetes over such a short period of time. And this increase was seen overall in both females and males, as well as in all age groups with the exception of the youngest age group, and in all racial ethnic groups with the exception of American Indians who have the lowest rates of type 1 diabetes.

So this is telling us and providing evidence that type 1 diabetes is increasing in the United States, and we still don't know why. Perhaps even more importantly, this was the first study that provided strong evidence that type 2 diabetes is increasing in the United States. As you can see here over an eight year time period, we found a 35% relative increase in the prevalence of type 2 diabetes. This was true overall. It was true in females and in males, with rates higher in females than in males, and it was true in younger and older children, with obviously rates are higher in older children. And if we look when we looked at increases by race ethnicity, the increase was significant in non-Hispanic white children, in African American children, and in Hispanic children, with no significant increases in Asian-Pacific Islanders and in American Indians.

This is an interesting observation. The prevalence remains the highest in American Indian children but we did not detect a significant increase over this time period in American Indian children. This may be due to a variety of reasons. Perhaps we've reached a plateau in this high-risk ethnic group. It might be good if that's the case, but we don't know yet until we analyze our incidence data. Perhaps we had a smaller sample of participants. It is in fact our smallest sample of participants because we are mostly focusing on some selected American Indian reservations in the southwest, and a few other American Indian kids that are included in the locations where the study exists. We need to continue to follow up these children to really understand whether type 2 diabetes will continue to increase or not in American

Indian kids, as well as in the other racial ethnic groups. The steepest relative increase in type 2 diabetes happened actually in Hispanic children.

So based on these data, the CDC and the SEARCH study has calculated the burden of diabetes in U.S. youth. Applying our prevalence data and incidence data to the U.S. Census denominators, we estimated that in 2009, approximately 191,000 youth in the US had physician-diagnosed diabetes, almost 167,000 of them type 1, and 20,000 of them had type 2 diabetes, with a smaller number having other types such as secondary forms of diabetes or genetic forms of diabetes. And still based on this data, we estimated that about 18,400 youth are diagnosed annually with type 1 diabetes in the United States, and 5,000 youth are diagnosed with type 2 diabetes each year.

Our colleagues from the CDC have used the SEARCH data to project the number shown here in bars, and the prevalence shown here as a line of type 1 in blue and type 2 diabetes in red, in people less than 20 years from 2010 to 2050. And based on their projections, which are based on the SEARCH data, there is a daunting expectation that the number of kids with type 1 diabetes will increase from less than 200,000 today to almost 600,000 in 2050, and the numbers of kids with type 2 will increase from about 20,000 today to almost 80,000 in 2050. So, these are daunting projections because if we don't do anything about this, this is going to be a scary picture. And the healthcare system has to be prepared to take care of these kids.

Okay. I'm going to switch from numbers and burden and prevalence and incidence to talk a little about the SEARCH contribution in other areas of pediatric diabetes. Remember, I started by saying it was hard and it's still hard for providers and for researchers and for families to determine what type of diabetes a child has. So defining diabetes type was a major aim of SEARCH ever since we started. Especially now with increasing obesity, youth with type 1 diabetes are overweight and obese, no longer skinny as they used to be 50 years ago, and this causes confusion about a correct diagnosis of diabetes type and, therefore, the treatment that such kids are supposed to have.

So what we did in SEARCH was to use two etiologic markers of diabetes type -- autoimmunity and insulin sensitivity -- to define etiologic groups or etiologic categories of diabetes. So we used autoimmunity based on measuring, in all our participants, two diabetes autoantibodies, IA-2 and GAD65. And we used insulin sensitivity which we did not measure directly because it's hard to measure that directly, but we assessed or we estimated insulin sensitivity using an equation that we've developed and validated against hyperinsulinemic-euglycemic clamps in a sample of SEARCH participants with type 1, type 2 diabetes, and controls from Colorado.

So this formula, estimating insulin sensitivity, is based on waist circumference, hemoglobin A1c and triglyceride levels, and it explains almost 70% of measured insulin sensitivity in the clamp study.

We then took this insulin sensitivity estimate and categorized it as insulin resistant if kids had an insulin sensitivity index below the 25th percentile for, and NHANES, non-diabetic children, or insulin sensitive if this index was above the 25th percentile. So then using autoimmunity and insulin sensitivity and insulin resistance, we were able to define these four mutually exclusive etiologic groups: autoimmune sensitive, autoimmune resistant, non-autoimmune sensitive, and non-autoimmune resistant. And we also looked at clinical, metabolic, characteristics of kids in these four groups including genetic predisposition for type 1 diabetes. And our conclusions are reflected here on the next slide, that the autoimmune sensitive group or the non-autoimmune resistant groups align pretty well with the traditional descriptions of type 1 or type 2 diabetes.

The autoimmune resistant group is perhaps the group that other providers and researchers have referred to as hybrid or double diabetes because it has both autoimmunity and insulin resistance or obesity. And we think that it likely represents individuals with autoimmune diabetes who are obese. Of interest, the distribution of HLA genetic susceptibility to type 1 diabetes in this group was identical to

that of kids with autoimmunity and insulin sensitivity which makes us think that this is not a new form of diabetes. This is simply type 1 diabetes in overweight and obese kids.

Then the other interesting group was the non-autoimmune sensitive group. They don't have autoimmunity. They don't have insulin resistance. Why do they have diabetes? Well, we think that this represents an etiologically mixed category, and in this group, further testing for determining diabetes type is needed. Remember, we just had two autoantibodies that we measured in the SEARCH population. Now, there are three or four such autoantibodies available. We did not have the ZnT8, a novel diabetes autoantibody at the time. And in a pilot study when we measure presence of ZnT8, we were able to reclassify a large proportion of kids in this group as having autoimmune diabetes. So we think that a lot of kids in this group, in fact, have undetected autoimmune diabetes. Then the genetic MODY forms of diabetes were also mostly in this group of kids. Nevertheless, that's a group that requires further testing.

We also found that for the purpose of public health surveillance, the provider assignment of diabetes type agrees pretty well with our etiological assessment. So going forward, we are more comfortably relying on a provider diagnosis of diabetes because we have evidence that this aligns well with etiological assessment.

So based on these findings, we have been proposing this algorithm for a classification of pediatric diabetes. So in the presence of autoantibodies, and I'm including here all antibodies if possible, including the fourth or third or fourth generation novel autoantibodies in the presence of such antibodies, a diagnosis of type 1 diabetes can be made regardless of obesity or family history or other clinical things. If no autoantibodies are detected and the kids are obese with a large waist circumference or people can use our equation to determine insulin resistance, then a diagnosis of type 2 diabetes can be made.

For the group in between, with no antibodies, and insulin sensitive, normal waist circumference, additional testing might be necessary, either genetic testing for a diagnosis of MODY, or assessment of other causes of diabetes, or other genetic factors, or maybe more careful assessment of autoantibodies and autoimmunity.

Another field in which SEARCH has made substantial contributions is describing the characteristics of youth with diabetes. What you see here is the prevalence of social economic indicators, low income and parental education in kids with type 1 and type 2 diabetes by race ethnicity. As you can see, there is a higher prevalence of poverty and lower prevalence of highest parental education in kids with type 2 that in those with type 1 diabetes. That is especially true in minority children including American Indian and African American children. This shows the prevalence of overweight and obesity by type and race ethnicity. Not surprisingly, kids with type 2 are almost entirely obese or overweight, but a sizable proportion of children with type 1 diabetes, as I was saying earlier, are now overweight and obese, and no longer the skinny type 1 typical presentation.

This shows the prevalence of selected health behaviors and it's shown as less than five servings of fruits and vegetables a day and low physical activity, less than the recommended 60 minutes a day amount. As you can see, this prevalence actually of unhealthy behaviors is quite high, and it is high in both type 1 and type 2 diabetes, and it's high across all racial ethnic groups indicating an urgent need that really is spanning across types of diabetes and racial ethnic groups to improve these health behaviors.

SEARCH contribution in the field of quality of care. This shows the prevalence of glycemic control; poor glycemic control, defined here as an A1c higher than 9%. This is really very poor glycemic control. As you can see, there is a marked disparity here in the proportion with poor glycemic control across racial ethnic groups with minority children especially, African Americans again, and Native

American children with either type of diabetes, having a very high prevalence of poor glycemic control. Fifty percent of American Indian kids with type 1 or type 2 diabetes have very poor glycemic control. This is again, an urgent need that has to do with processes of care and the care we provide to our kids with diabetes.

The next slide shows the percentage of youth reporting receipt of various test measurements, whether they have these things measured as required by ADA Guidelines. This is not by type or by race ethnicity. As you can see, maybe blood pressure measurements are done pretty frequently but there is more to do in terms of A1c testing, eye exams, and microalbuminuria testing.

Moving on to risk of chronic complications, this shows the prevalence of cardiovascular risk factors by race ethnicity. It doesn't break it down by type, the diabetes type here, and as you can see here, a very high prevalence of high waist circumference, high triglyceride levels, low HDL, high blood pressure, again, a higher prevalence in minority children and especially, in American Indian children.

Prevalence of elevated albumin-creatinine ratio, microalbuminuria, crude and adjusted for duration and age, about 10% in type 1, close to 35% in type 2 diabetes, a little bit higher again, in minority children, African American and American Indian children although not shown here.

Prevalence of other microvascular complications from a pilot study in SEARCH. SEARCH is conducting now a much bigger exploration of this topic. But from that pilot study, prevalence of retinopathy, 17%, in type 1 kids, 42% in type 2 children, and peripheral neuropathy assessment with the Michigan Neuropathy Screening Instrument, again, much higher in youth with type 2 diabetes. All these data suggesting that perhaps type 2 diabetes in kids is even more aggressive than type 1 diabetes. I'm going to go pretty fast through the example of the SEARCH-Navajo Study as an example of American Indian participation in SEARCH.

Who's eligible? Patients with physician-diagnosed diabetes, same criteria as for the larger SEARCH study, active users of the Indian Health system, users in the past three years, not active duty in military, not institutionalized in prevalent years or at diagnosis. So, very similar definitions to the rest of the SEARCH study.

So what we did in Navajo was, we worked with the Indian Health Service units as well as with those who were 638-ed to first identify the denominator and number of kids in each of these service units who were present, who were active IHS users in the prevalent or incident years. Then within those denominators, we identify in the RPMS, kids with diabetes prevalent in 2001 or incident in 2002. You have the numbers here highlighted. And then what we did was to go back to medical records at the time. Those were hard records, nowadays some of them are electronic, to validate the diagnosis of diabetes. As you can see, that effort, that act kind of cut almost in half the sample of kids with diabetes that was identified because a lot of these children who were supposedly quoted as having diabetes in the RPMS were miscoded and did not really have a diagnosis of diabetes.

So that's an important point that I wanted to make that we need to follow the electronic billing system for example with actual validation of diabetes. In Navajo, these are the data, prevalence of diabetes in 2001 for 1,000 among Navajo youth. In younger kids, most have type 1 diabetes. In the older kids, most have type 2 diabetes.

These data translate into one in 2,640 Navajo kids had diabetes in 2001, and 1 in 664 older Navajo kids had diabetes in 2009, so more in the older age group. Comparing these data with previously published data, Kelly Acton published a paper a few years before the SEARCH data were published in American Indian and Alaska Native youth based on RPMS with no medical record validation. The numbers in that publication are slightly higher than those observed by SEARCH in Navajo, perhaps because she

included a larger number of tribes, but also perhaps, because there was no medical record validation in that study.

These are data on the incidence of diabetes in Navajo youth for 100,000 per year. Again, in younger kids, mostly type 1 diabetes, in older kids mostly type 2 diabetes, with 1 in 45,000 Navajo youth age less than 10 developing diabetes annually, and 1 in 3,400 Navajo youth developing diabetes annually in the older age group.

Some of the characteristics of Navajo youth with diabetes by type, as you can see here, fasting c-peptide is higher in type 2 versus type 1 diabetes. A higher proportion has elevated CES-D scores. This is an instrument that screens for depressive symptoms. So more kids with type 2 than those with type 1 have some evidence of depression. High waist circumferences is higher in kids with type 2 than in type 1. High blood pressure, more in type 2 than in type 1, higher prevalence of microalbuminuria, higher triglycerides, lower HDL cholesterol, poor glycemic control, about the same in both groups.

The following slides show some treatment patterns of Navajo youth with type 1 and type 2 diabetes. You can see for type 1 diabetes, one or two injections of insulin a day, three and more in 66% of cases but no kids at the time was on pumps, which contrasts with the data we have on other SEARCH locations where a larger proportion of children are on insulin pumps.

For type 2 diabetes, a combination of insulin and oral agents is present, but only 70% of kids with type 2 diabetes are on metformin. Lipid-lowering treatment is 5.2% in type 2 diabetes. Nobody in type 1 diabetes, these data are similar to those that we've seen in the rest of the SEARCH study. And 25.8% of those with type 2 diabetes were on anti-hypertensive treatment, perhaps a little more than we've seen in the rest of the SEARCH study, and nobody among the kids with type 1 diabetes.

Okay. So SEARCH is now in its 14th year of life and it's planning for the future. We're planning to embark in what we call SEARCH 4, and we would like to continue some of the work that we've done over the past 14 years. In what we call our Registry Study, we want to continue to conduct sentinel surveillance of diabetes over the next five or ten years, because we think that the SEARCH registry can be utilized to provide national estimates of prevalence, incidence, projections, temporal trends, mortality without the need for really, a truly national system. I did not mention, but SEARCH is conducting at this point in time, a mortality study as well, by diabetes type and by race ethnicity, and some interesting results will likely be published soon.

Now, as we are thinking for the future, and as I was presenting the example of Navajo participation in SEARCH, one question that we have, and we are probably trying to work this through a little bit more, can SEARCH be expanded to include other American Indian tribes? Perhaps through a stronger collaboration with the IHS to implement the model that we have with Navajo elsewhere, perhaps as broadly as at the entire IHS level.

That would be important because right now, our sample of American Indian children is relatively small and it may not be truly representative of all American Indian children in the United States. We want to continue to do this to address some major research questions such as, will the incidence of type 1 diabetes continue to rise? Or will there be a leveling off as most recently reported in Scandinavian countries who have the highest incidence and prevalence of type 1 diabetes in the world. Similarly, will the incidence of type 2 diabetes, will it continue to rise or will there be a leveling off, particularly in the highest risk groups? We can only answer these questions if we continue to conduct surveillance of pediatric diabetes.

For the cohort study, we would like to continue this longitudinal follow-up of the SEARCH inception cohort of young adults with type 1 diabetes. In fact, there is no such cohort in the United States that

brings together both types of diabetes at the same time in the same evaluation structure. Most studies either include type 1 or type 2 diabetes but no major study brings them both together.

We would like to try to address some of these questions. What is the clinical evolution of acute and chronic early complications of diabetes among youth and young adults with type 1 or type 2 diabetes? Is, indeed, type 2 diabetes more aggressive than type 1 diabetes? And if so, what are the drivers of such early complications of diabetes? And do these drivers differ for type 1 and type 2? And I'm talking here about clinical care, metabolic risk factors, but also behavioral, socioeconomic, societal risk factors comprehensively.

I'm going to end this with a different study, this is not SEARCH, but it is a study that we're currently conducting because of SEARCH, because of how SEARCH has informed the development of such interventions. The study is called the "Tribal Turning Point" and it addresses the issue of reducing the risk of type 2 diabetes in American Indian youth. It is a partnership between my colleague at Chapel Hill, Beth Mayer-Davis, my co-chair in SEARCH, myself, at the University of Colorado Denver, working with two American Indian nations, the Eastern Band of Cherokee and the Navajo Nation.

We're doing the study because this is a compelling need in American Indian community. SEARCH has told us that American Indian youth have the highest incidence and prevalence of type 2 diabetes, and type 2 diabetes is perhaps more aggressive in children. There's a high overweight prevalence in American Indian children and adults. We're also doing this because we have evidence from previous efforts that we might be successful. We have strong efficacy data from efforts to prevent type 2 diabetes in adults with lifestyle changes, the Diabetes Prevention Program chiefly, which has been translated to Native communities, the Native Lifestyle Balance Program, a close modification of DPP to be applied or that is applied to American Indian group-based community settings with some success.

Then, we have data from interventions in youth that are actually not very encouraging with mixed results. We have the HEALTHY Study and the Pathways Project that were not quite that successful. So that made us think that we may be more successful with a multi-component program that provides physical activity, support for dietary changes involving key community partners and especially families. So we designed the Tribal Turning Point with the overarching goal to develop, deliver and evaluate a novel, three-component intervention designed to reduce risk factors for type 2 diabetes in Cherokee and American Indian youth.

We designed this intervention with the goal of an eventual broad, sustainable dissemination to other high risk communities. This is a pilot study, a two-year pilot study. First thing is to further develop the intervention through a community-based participatory research process. We're at the end of that first year. We started the second year which aimed to implement this intervention in an eight month pilot and feasibility trial in Cherokee and Shiprock.

A little bit about the intervention development, so through focus groups in the two communities and through working with people locally, we developed the intervention. It has three components: active learning classes, a total of 10 classes with hands-on activities, physical activity and goal tracking. It has a toolbox component, materials and resources to be used as needed by staff and coaches following the Social Ecological Model. The third component is motivational interviewing, the person-centered counseling technique used to strengthen a person's motivation and commitment for change by using and building problem-solving skills.

The basis for the physical activity component of the intervention is at least 60 minutes per day, fitness-focused, age appropriate, culturally relevant, suitable for overweight kids. The basis for diet and weight loss is the traffic light guide with green, yellow, and red foods, and the 5-2-1-0 Campaign, which you probably are familiar with. We are in the second year of this pilot study, so we finalized, we refined the intervention. We studied the pilot study per se in August with baseline measurement and

randomization. Then we are now in the period where we are conducting the 10 active learning classes with three MI sections and toolbox resources if needed, some booster classes in January to April, and by May of next year, we should conduct the end of study measurements, analyze the data, and provide some results.

As I said, there are two sites participating here, Cherokee, North Carolina and Shiprock, New Mexico. We've enrolled our children. Enrollment went great. There was a lot of interest. It was amazing how much interest there was in both communities. Our outcomes are going to be change in BMI, change in fasting insulin as primary outcomes, with A1c changes and fasting glucose changes as secondary outcomes, and process outcomes, intervention, acceptability in changes in diet, physical activity behaviors.

So I went very fast through all this. I want to thank my colleagues in SEARCH, as well as all youth and families and providers participating in the SEARCH study whose participation made the study possible and I am happy to address some of your questions now.

Kelli Begay:

Great. Thank you Dr. Dabelea, this is Kelli Begay. Unfortunately, Jan had some technical issues with the audio. So I'll go ahead and feed you those questions that came through the chat so far. There was one that was earlier in the presentation. Someone wants to know, can your equation for insulin sensitivity be used outside your population?

Dana Dabelea:

Yeah, absolutely. We would be delighted if providers outside SEARCH will start using the equation and to facilitate that, we are now developing a web-based formula that can be accessed through our website that will permit the providers to use the equation and assess insulin sensitivity and determine diabetes type.

Kelli Begay:

So a follow-up question to that is, do you know the website by chance right now, or is that coming?

Dana Dabelea:

I'm talking about the SEARCH website, it's going to be on the SEARCH website. It's not there yet but we are planning to do that.

Kelli Begay:

Okay. Great, thank you. Another question, this was around slide 24. So I don't know if you memorized your slides by number, but someone asked if the American Indian population had the lowest obesity prevalence.

Dana Dabelea:

Yeah, interestingly, the differences were not significant, but the American Indian participants with type 2 diabetes did not have a higher prevalence of obesity than other racial ethnic groups participating in SEARCH who have type 2 diabetes. In other words, kids with type 2 diabetes are generally overweight or obese regardless of race ethnicity. That's what that slide is saying. It's not saying that American Indian kids are not more obese than white kids. But kids with type 2 diabetes, regardless of race, are similarly obese.

Kelli Begay:

Great, thanks. That's a great clarification there. Another question is, what is the prevalence of the selected health behaviors in U.S. children without diabetes or overall?

Dana Dabelea:

That's a very good question, as you saw, the prevalence of unhealthy behaviors was quite high regardless of diabetes type and race ethnicity, and it's as high in non-diabetic children as well. This is unfortunate and really says more about behaviors in youth in this country than about behaviors in youth with diabetes per se.

Kelli Begay:

Thank you. Another question, what makes the diabetes onset in younger population more aggressive? Is it related to more insulin resistance or is there rapid beta-cell destruction?

Dana Dabelea:

Yeah, that's another great question, that I'm not sure that I know the answer to, because to answer that question, you would need to follow these kids until they develop complications to really understand that whether their disease is more aggressive or not, as compared to the disease that exists in adults, or that exists with an adult diagnosis of diabetes.

We have very, very few if any cohorts of kids with diabetes that were followed long enough to answer this question. So at this time, I can only say that I think it's duration of diabetes. If they are diagnosed at an earlier age, they're going to have more years of diabetes than if they're diagnosed as adults and therefore, by age 30 or 40, if they were diagnosed at five, they might have much more complications and problems. But it could also be that the beta-cell destruction is more aggressive at a younger age. That's certainly the case with type 1 diabetes. The younger you're diagnosed, the more likely is to be diagnosed with no beta-cell function.

Kelli Begay:

Great. Thank you.