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# Obesity and Type 2 Diabetes in Children: Epidemiology and Treatment

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# Abstract

The incidence of overweight and obesity among children has increased dramatically in recent decades, with about one-third of children in the U.S. currently being either overweight or obese. Being overweight in early childhood increases risk for later obesity. There is evidence for the efficacy of family-based behavioral treatment to control weight and improve health outcomes. Obesity-related health risks have been documented, including metabolic syndrome. There is also increasing incidence of type 2 diabetes (T2D) among youth in recent years, with obesity and family history of T2D generally present. Lower income and ethnic minority status are associated with both obesity and T2D in youth. Most youth with T2D do not achieve optimal glycemic control, and are at high risk for later health complications. Obesity and T2D represent significant public health issues with potentially great personal and societal cost. Research addressing the prevention of obesity and T2D among youth is urgently needed.

#### Keywords

Children; Adolescents; Overweight; Obese; Type 2 Diabetes; Treatment; Prevention

# Introduction

The purpose of this article is to review the epidemiology and treatment of obesity and type 2 diabetes (T2D) in children and adolescents, as well as consider other relevant factors such as etiology and behavioral and psychological correlates. In recent years, rates of pediatric obesity have increased dramatically, and T2D in youth has also been diagnosed more frequently and at younger ages than typically seen before historically. With the current generation of youth in the United States being significantly more overweight than previous generations, and the fact that T2D is increasingly apparent at younger ages, both of these conditions represent significant public health issues.

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Compliance with Ethics Guidelines

Conflict of Interest

Elizabeth R. Pulgaron and Alan M. Delamater declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent

This article does not contain any studies with human or animal subjects performed by any of the authors.

### **Obesity in Children and Adolescents**

#### Definition

Obesity is typically defined as having an excess of body weight caused by a chronic caloric imbalance with more calories being consumed than expended each day. Body mass index, or BMI, is a measure used to classify children as overweight or obese. A z-score is computed using the child's weight and height and the score is then compared to an age and gender percentile-based norms to determine weight status. The Center for Disease Control uses the 85% ile and 95% ile as the cutoffs for classifying a child as overweight and obese, respectively.

#### Epidemiology

Recent estimates from the National Health and Nutrition Examination Survey indicate that approximately one-third of children in the United States are overweight or obese, with approximately 17% meeting criteria for obesity [1\*\*]. Worldwide, approximately 43 million preschool-aged children have been estimated to be overweight and obese, and 92 million are considered to be at risk of overweight [2]. Children from African American and Hispanic cultures are at an increased risk for being overweight or obese [3]. A recent national longitudinal study in the US indicated that 12.4% of children in kindergarten were obese and another 14.9% overweight; overweight 5-year-olds were four times more likely than normal weight children to become obese later in childhood at age 14, and among children who later became obese, half were overweight at baseline and three-quarters were above the 75<sup>th</sup> %ile for BMI [4\*\*].

#### Comorbidities

Children who are obese are at a significantly elevated risk for adverse health outcomes including both medical and psychological problems [5]. The most common medical comorbidities associated with obesity include metabolic risk factors for T2D including high blood pressure, high cholesterol, impaired glucose tolerance, and metabolic syndrome [6,7]. Orthopedic problems, sleep apnea, asthma, dental problems, and fatty liver disease are also common comorbidities of obese children and adolescents. Behavioral factors have significant effects on metabolic risk. Research has shown that youth who do not meet guidelines for dietary behavior, physical activity and sedentary behavior have greater insulin resistance than those who do meet guidelines [8].

Psychosocial correlates of obesity include internalizing and externalizing disorders, ADHD, problems related to body image, reduced quality of life, low self-esteem, social isolation and discrimination [5,9\*,10]. Depressed mood has been associated with greater risk of obesity and higher BMI [11]. The short and long-term medical and psychosocial effects of childhood obesity have adverse consequences including increased morbidities and early mortality in adulthood [12]. A prospective study of obese adolescents revealed that as young adults, women particularly had an increased risk of social and economic difficulties [13].

# Etiology

Obesity has been attributed to various factors including genetics, environment, metabolism, behavior, personal history of obesity, culture, and SES [9\*]. The origins of obesity can be traced to early adiposity rebound, which refers to the time at which young children's BMI begins to increase after reaching their lowest level of body fat (typically around the age of five or six). Children who experience adiposity rebound beginning at age three years tend to have increases in mean BMI from age three to adolescence which often extends into adulthood [14\*, 15].

The debate between nature and nurture also applies to the topic of obesity, and few prospective studies are available to help disentangle the two factors [16].. Childhood overweight status has been associated with parent [17] and grandparent overweight status [18]. Children born to overweight or obese mothers are more likely to be overweight by the age of four years old even if their BMI is within the average range at the age of two [19]. A longitudinal study of girls indicated that compared with families in which neither parent was overweight, if both parents of a girl were overweight the girl was eight times more likely to be overweight by the age of 13, even after controlling for the girls' BMI at the age of five [20]. Twin and adoption studies, with the ability to attribute familial similarity to genetic and environmental effects, support both genetic and environmental factors on childhood BMI, with the influence of environmental factors dissipating in adolescence [21]

Other aspects of the family environment are also highly influential. Children of single-parent homes and those with high family stress have been found to be more overweight than those from two-parent homes and homes with less familial stress [22]. Parents' knowledge about nutrition and physical activity has also been found to be very strong predictors of children's weight status [23]. In one study of 812 school-aged children, parenting behaviors and parental BMI were stronger predictors of children's BMI than school and community influences [24].

Characteristics of the community have also been found to contribute to high rates of obesity. Compared to our ancestors, current environments provide an overload of opportunity to consume high density and high fat foods. Features of the built environment, including access to parks, supermarkets, and convenience store hours, have been found to moderate treatment effects of obesity interventions [25]. Proximity of a person's home to fast food restaurants has been associated with increased obesity rates [26].

Consumption of healthy food and energy expenditure in the form of physical activity are imperative to maintaining healthy weight. Results from the 2011 Youth Risk Behavioral Survey conducted in the United States indicated that among high school students nationwide, 22.5% reported eating fruit or drinking 100% fruit juices three or more times a day or more, and only 15.3% reported eating vegetables three or more times per day in the past week. During an average school day, nearly one-third (31.1%) reported playing video or computer games for 3 or more hours and about 50% reported not engaging in 60 minutes of physical activity 5 days a week in the last week [27]. One study reported that 40% of children between the ages of 1 and 5 years old had a television set in their room and the odds ratio of being overweight was 1.06 for each additional hour per day of television or videos

seen [28]. Another study estimated that children of parents who are obese watch about 30 minutes more of television per day [29].

**Cultural Factors**—Increased risk for obesity among ethnic minority children may be explained in part by behavioral factors. Research with Mexican-American children, for example, has shown they have greater body fat, lower physical fitness and more sedentary lifestyle; in addition their diet is more likely to be unhealthy, including a greater percentage of calories from fat and saturated fat, and less consumption of fruits and vegetables [30]. Another study with Mexican-American children demonstrated early risk factors for metabolic syndrome, including high levels of body mass index, insulin, glucose, triglycerides, and systolic blood pressure, as well as lower HDL cholesterol [31]. Research with African-American children has demonstrated greater risk for T2D, with lower insulin sensitivity and higher insulin secretion than white children, after controlling for body mass index and/or visceral fat accumulation [32].

Differences in physical activity and sedentary behavior help explain ethnic and socioeconomic disparities in obesity rates of children. Research findings indicate ethnic minority children have higher rates of sedentary activity and get less physical activity than white children students in the United States [33, 34]. Living in low-income neighborhoods has also been associated with more sedentary behavior and less physical activity [35]. School environments affect physical activity in youth, as research has shown children in high socioeconomic (SES) schools have more regular physical education classes than children attending low SES schools [36]. The evidence therefore indicates that environmental factors associated with urban and low-income neighborhoods increases the likelihood of low rates of physical activity among minority and low SES children.

Recent research on disparities in physical activity has focused on the "built environment," including neighborhood characteristics such as amount of green space, degree of urbanization, residential/commercial land use, and transportation systems [37]. Ethnic minority youth have less access to safe facilities in their neighborhoods in which to be physically active [38]. Low SES neighborhoods often lack sidewalks and are unsafe, factors that are associated with higher rates of obesity [39].

There are also many barriers to a healthy diet for low SES and ethnic minority youth. For example, research has documented that youth living in low SES neighborhoods have less access to supermarkets providing fresh fruits and vegetables, high fiber bread, and low fat milk [35]. Convenience stores or bodegas in these environments are more often utilized by families, providing foods which have higher concentrations of sodium, fat, and processing. With fewer supermarkets, not surprisingly there are more fast food restaurants concentrated in low income neighborhoods that have more ethnic minority children [40].

#### Treatment

The U.S. Preventative Services Task Force (USPSTF) recommended in 2010 that children be screened for obesity by the age of six years and if they meet criteria they should be offered moderate to intense (25 hours or more) diet, physical activity, and behavioral childhood obesity treatments [41\*\*]. However, given the fact that obesity in children at the

age of five years predicts later obesity [4\*\*], screening and treatment for obesity should occur even earlier in childhood. There are a number of approaches for the treatment of overweight children, including family-based behavioral lifestyle intervention, internet-delivered interventions, residential interventions, medical interventions, and school-based interventions.

Family-based Intervention—Family-based behavioral interventions have been shown to be efficacious for overweight children, with significant weight loss maintained even ten years after treatment [9\*, 42]. Family-based interventions for weight management include nutrition and physical activity education, self-monitoring of dietary intake and physical activity, goal-setting, stimulus control techniques, and training parents in behavior modification for children's reduced caloric intake, increased physical activity, and reduced sedentary behavior. Sessions are often attended by multiple family members and the unit of change is the family, not just the child. Recent reports comparing alternative family-based obesity interventions for children have found significant improvements for treated children. For example, Steele and colleagues recently compared the effects of a multi-component family-based behavioral outpatient program to a brief family intervention in overweight children and adolescents [43]. Significant reductions in BMI and improved quality of life occurred for both treatment groups at post-treatment and maintained at one-year follow-up for the children, but not for the adolescents in the study. Similarly, both prescribed and selfdirected approaches to family-based obesity treatments have resulted in significant weight loss up to two years after treatment [44].

Effective treatment of obesity is particularly needed for ethnic minority youth, who are at increased risk not only for obesity but also for T2D. Ethnic minority children and their parents also are more likely to drop out of treatment programs for obesity [45]. A recent randomized controlled trial was conducted with ethnically diverse youth in an urban setting in which a family lifestyle program was delivered over a one-year period and follow-up continued for another year. At the end of treatment, children who received intensive family intervention had decreased zBMI as well as improved lipids and reduced insulin resistance. Although there was significant attrition, results indicated that the benefits of family-based intensive lifestyle intervention were sustained over time [46].

**Internet-delivered Intervention**—Besides family-based behavioral programs for weight management, researchers have begun to adapt therapeutic interventions using the internet. The internet is often used for health information and has great potential for the delivery of weight control interventions, thereby increasing reach to the population of overweight youth. Traditional behavioral modification techniques used in face-to-face interventions have been adapted to an online format. Web-based modules are used to deliver information, promote individually-tailored goals, and provide personalized feedback on progress. Monitoring target behaviors and attainment of goals are key components of successful internet-based programs. Several recent reports suggest the efficacy of web-based weight loss interventions for use with pediatric populations. For example, one study of high school girls enrolled in a health class, demonstrated decreased fast food consumption and increased physical activity

for those students randomized to five internet-based modules which supplemented the health curriculum [47].

Internet-based interventions have become increasingly interactive and personal through the use of telemedicine. This modality of treatment has been used with rural patients or those who have difficulty accessing clinics in person. Some successful telehealth obesity interventions have been compared to in-person interventions. For example, improvements in zBMI, nutrition, and physical activity were found in rural youth upon completion of a telemedicine intervention program [48]. Recently, a five- year comparison of young patients involved in a telemedicine weight management clinic versus a face-to-face weight management clinic indicated that for patients who attended clinic more than once, those in the telemedicine group demonstrated substantially more improvement than those in the face-to-face group on nutrition, physical activity, and screen time outcomes [49]. In a pilot test of an interactive, family-based internet intervention for overweight children, those who utilized the website more frequently had improvements in zBMI and healthy eating over one month [50]. Parents are satisfied with receiving obesity interventions for their children via telehealth [51].

**Residential Treatment**—A more drastic and intense approach to obesity intervention involves hospitalization or residential treatment, sometimes described as immersion treatment, to implement specific behavior change techniques. Immersion interventions remove children from their home environments and place them in educational and therapeutic environments for an extended period of time. These interventions include diet, physical activity, nutrition education, behavior modification, and some even have a family component [52]. A recent review of 22 immersion studies indicated positive reviews of these programs. Percent-overweight (Percent-overweight = ([Reported BMI / 50<sup>th</sup> percentile BMI]–1) × 100) was used as a way to standardize results from the literature. Results indicated that on average, participants decreased percent-overweight by 23.9% during treatment and by 20.6% at follow-up [52]. One report of 122 obese youth who participated in a 10-month inpatient program indicated that youth lost 49% of their weight after 10 months, and at a 14 month follow-up they maintained a 32% weight loss from baseline; improved dietary habits and psychological well-being were also reported [53].

The limitation of many of the inpatient or immersion studies is the lack of control groups and randomization. One study attempted to control for this by comparing participants who attended a four week residential weight loss camp to those who attended an eight week residential weight loss camp. All campers experienced significant reductions in zBMI and systolic blood pressure, and compared to those in the four week group, campers in the eight week group experienced larger reductions across outcomes [54].

**Medical Treatments**—Three of the most common drugs in recent adolescent obesity treatment research include sibutramine, orlistat, and metformin. Viner and colleagues [55] conducted a meta-analysis of randomized controlled trials of obesity treatment drugs for adolescents. Most of the trials identified were of sibutramine and a few with orlistat. Results indicated reductions in BMI for both treatments when combined with behavior intervention: 2.20 kg/m<sup>2</sup> for sibutramine and 0.83 kg/m<sup>2</sup> for orlistat. Other benefits of pharmacological

treatment included smaller waist circumference, lower triglyceride levels, and high density lipoprotein-cholesterol; however, serious side effects were noted with medication use including increases in systolic and diastolic blood pressure, and higher pulse rates for sibutramine, and a high prevalence of gastrointestinal adverse effects for orlistat.

Metformin has also been evaluated for the treatment of adolescent obesity. Three randomized trials with relatively small sample sizes provided preliminary support for the use of metformin in treating obese adolescents. Specifically, metformin treatment (from 8 weeks to 6 months in length) resulted in greater weight loss, reductions in BMI, and fasting insulin compared to control groups [56, 57]. Metformin, coupled with lifestyle modification, has demonstrated modest to moderate reduction in BMI in some short-term obesity studies [58], but the long-term effect of metformin on adolescent overweight is unknown. Larger and longer multi-site trials of this medication are needed to gain a better understanding of its effectiveness for weight control and potential side effects in pediatric populations.

Bariatric surgery is a viable option for extremely obese adolescents, especially those with multiple co-morbidities who have not responded to traditional behavioral and pharmacological interventions [59\*]. There are several types of bariatric surgeries; the most commonly used in adolescents are laparoscopic roux-en-y gastric bypass, laparoscopic adjustable gastric banding, and laparoscopic sleeve gastrectomy. Each surgery has its unique advantages and risks and the most appropriate type of surgery will depend on the presentation on a given patient.

One study of adolescent patients from the United States Bariatric Outcomes Longitudinal Database indicated that those who underwent gastric bypass surgery lost almost double the amount of weight one year post surgery compared to those who had the adjustable gastric band procedure [60]. There is also some evidence to support having surgery in adolescence versus adulthood to maximize improvements in medical and psychological health [61], but the long-term outcomes of bariatric surgery in youth are still to be determined. Well-controlled larger studies of adolescent bariatric surgery are needed to determine its full potential in obesity treatment.

**School-based Intervention**—Because children spend so much of their day in the school setting, schools provide an opportunity for education about healthy lifestyles and may help to prevent obesity. Schools can also help inform parents about their children's obesity status through screening programs which are generally well received [62]. A large number of controlled studies have shown school-based interventions to have some success in improving children's dietary and physical activity habits, as well as improving their weight status [9\*].

Recent studies have also focused on school-based approaches to reduce obesity in order to prevent T2D. Grey and colleagues studied children at increased risk for T2D by virtue of their overweight status and family history of T2D [63]. Children were randomized by school to participate in a multi-faceted school-based educational intervention with or without coping skills training and health coaching to reduce T2D risk. Over the one year study period, students in both groups showed some improvements in anthropometric and

metabolic risk measures, but zBMI was not improved. Students receiving coping skills and health coaching evidenced greater improvements in total cholesterol, triglycerides, and two-hour glucose during OGTT.

Given the challenges of obesity treatment, school-based interventions may be especially critical for prevention of obesity and T2D. A comprehensive school-based intervention was evaluated in a national multi-site randomized controlled trial [64\*\*]. The study sample included 4603 6<sup>th</sup> graders who were followed until the end of 8<sup>th</sup> grade. The intervention group experienced environmental changes in the school setting including changes to school breakfast and lunch menus , increased physical activity, and behavioral change by increasing health knowledge through interactive games and goal setting. Intervention efforts were reinforced by social marketing . Baseline evaluation revealed increased risk factors for T2D among overweight children [65]. While the intervention did not result in greater decreases in the combined prevalence of both overweight and obesity, there were significant reductions in other measures of adiposity and metabolic risk, including zBMI, waist circumference, and fasting insulin.

#### Type 2 Diabetes in Children and Adolescence

#### Description

In T2D, hyperglycemia is the consequence of insulin resistance and beta-cell dysfunction. Peripheral insulin resistance occurs early in the disease course, and initially is compensated for by hyperinsulinemia. However, hyperglycemia results over time as the consequence of declining insulin secretion. T2DM has a multi-factorial etiology, including genetic, physiologic, and lifestyle-related obesity, with hypercaloric dietary intake, low rates of physical activity, and increased sedentary behavior. T2D in youth is characterized by have insulin resistance, and other features of metabolic syndrome are commonly present, including hypertension, hyperlipidemia, acanthosis nigricans, fatty liver disease, and polycystic ovary disease. [66, 67\*\*].

#### Epidemiology

Many studies have shown that T2D has increased dramatically in children and adolescents throughout the world in recent years [68\*,69]. The results of epidemiologic studies have shown the incidence of T2D in children and adolescents to have a range of 1-51/1000, depending upon ethnic group [70]. The highest rate is for 15-19 year-old North American Indians, where the prevalence per 1000 has been estimated as 51 for Pima Indians, 4.5 for all U.S. American Indians, and 2.3 for Canadian Indians; the prevalence of T2D increased six times from 1967-1976 to 1987-1996 for Pima Indian adolescents [70]. A more recent report showed that among 10-19 year-old youth in the U.S., the overall rate of T2D was 0.22/1000, but 0.42/1000 among ethnic minority youth [71]. Results from the U.S. SEARCH study revealed a rate of 8.1/100,000 10-14 year-olds, and 11.8/100,000 15-19 year-olds, with lowest rates among non-Hispanic white youth and the highest rates among Native American Indians [72\*].

The average age of onset of T2D in youth is 13 years of age [67\*\*, 73]. Before the mid-1990's, very few children with diabetes (about 1-2%) were classified as having T2D.

However, as obesity has increased in recent years, the incidence of T2D has increased to 25-45% of all youth diagnosed with diabetes [73,74]. In studies published in the late 1990's in Ohio [75] and California [76], youth diagnosed with T2D increased dramatically, accounting for 33-45% of all new cases of diabetes in those centers, with most of these youth being obese, ethnic minority, and having a positive family history of T2D. Similarly, rates of T2D among youth in the United Kingdom [77] and India [78] have been reported to be increasing rapidly in recent years.

T2D disproportionately affects adults with lower SES so it is not surprising that youth with T2D are also more likely to be from lower SES backgrounds [79]. Economic and ethnic disparities in youth with T2D seem to parallel the disparities in obesity among youth, with ethnic minority and low-income children more likely to be obese than white, middle class youth [80].

In summary, research indicates that T2D is being increasingly diagnosed in older children and young adolescents throughout the world [68\*; 69, 81). There is a great range of prevalence and incidence, with consistently higher rates among youth from Native American Indian, Hispanic, black, and southern Asian ethnic backgrounds. In Europe, while still somewhat rare, T2D is also increasing in prevalence. Besides obesity and family history of T2D, *in utero* exposure to hyperglycemia appears to be another risk factor for T2D [81].

#### Comorbidities

The most common comorbidity of T2D in youth is obesity [67\*\*, 70, 73]. There is a strong relationship between the increasing rates of obesity observed in recent decades with the increasing incidence of T2D among children and adolescents [66,70,81]. Studies indicate that over 85% of children with T2D are either overweight or obese at diagnosis [67\*\*, 73]. In a comparison of youth with type 1 and T2D, 96% of those with T2D, versus 24% of children with type 1 diabetes, were overweight or obese at diagnosis [82].

It is clear that poor glycemic control eventually results in serious health complications such as retinopathy, neuropathy, and nephropathy, and cardiovascular disease. Recent research has demonstrated that many youth with T2DM already have early signs of microvascular and macrovascular complications, hypertension, dyslipidemia, and fatty liver [83\*; 84\*]. For example, in the U.S. multi-site TODAY trial with 704 youth with a diagnosis of T2D of less than two years, at baseline, 80% had low HDL-cholesterol, 26% had systolic hypertension, 13% had microalbuminuria, 10% had high triglycerides, and most were obese (mean zBMI of 2.15) [85]. Glycemic control begins to deteriorate within two years after diagnosis [86]. The long-term prognosis of youth with T2D is not currently known, but it is estimated that these youth may have a loss of up to 15 years of life expectancy, and increased risk of serious health complications by the time they reach their 40's, depending on their level of glycemic control [87\*\*].

#### Lifestyle Behaviors

In general, research has shown less healthy lifestyle behaviors among overweight and obese youth than their normal weight peers, with more sedentary behavior, less physical activity,

and poorer dietary habits. Although there is less research on lifestyle behaviors of youth with T2D, the available findings indicate a similar pattern. An early report showed no regular physical activity, low fiber intake and high dietary fat intake among adolescents with T2D and their family members [88]. A more recent study of adolescents with T2D found they frequently overate, drank sweetened beverages, ate fast food, and had high rates of physical inactivity [89]. Another report found that youth with T2D, compared with age and BMI-matched youth without diabetes, had lower levels of cardiorespiratory fitness and less physical activity [90]. Similarly, a report from the TODAY study group found that youth with T2D were significantly more sedentary than obese youth from the NHANES cohort [91].

#### Treatment

The major goal of treatment is to achieve normoglycemia. To achieve this, daily oral medication (metformin) and sometimes insulin is prescribed [67\*\*], along with daily monitoring of blood glucose, as well as other daily medications to treat various comorbidities.. Metformin, an insulin sensitizer, was shown to significantly improve glycemic control in youth with T2D [92]. Metformin and insulin are the only medications currently approved for use in youth with T2D, although a number of other medications are being considered [93\*]. More controlled studies are needed for the selection and initiation of specific oral medications and insulin [67\*\*, 94].

A key issue in treatment is patient and family education to improve medication adherence and lifestyle modification in order to reduce obesity [94]. However, management of T2D is clearly challenging for clinicians. In a survey of physicians caring for youth with T2D, several problems were noted, including high risk behavioral lifestyles, behavioral and psychological problems, decreased motivation for self-care, and cultural barriers [95]. Because most youth with T2DM are overweight, it is essential for them to lose weight by focusing on improving dietary intake, increasing physical activity, and decreasing sedentary behaviors. Because family influences are so important for children's lifestyle behaviors, such interventions should involve parents and other family members [88].

While there is little evidence for the optimal treatment of T2D in youth [93\*], it is clear that both medical and lifestyle intervention is needed, as recommended in the consensus guidelines published by the International Society of Pediatric and Adolescent Diabetes (67\*\*). The TODAY trial is the largest randomized controlled trial available to examine treatment of T2D in youth [96\*\*]. In this national multi-site study, 699 10-17 year-old youth with mean duration of T2D of 7.8 months, were randomized to either monotherapy with metformin, metformin plus rosiglitazone, or metformin plus a family lifestyle intervention program focused on weight loss through modification of eating and physical activity. The primary outcome was loss of optimal glycemic control, which was defined as having a glycosylated hemoglobin A1C of 8% or more for at least six months, or metabolic decompensation requiring use of insulin.

Over a mean follow-up of 3.9 years, the study findings indicated that nearly half of the patients had durable glycemic control with metformin alone; metformin plus rosiglitazone resulted in better glycemic control than metformin alone, but the addition of lifestyle

intervention to metformin did not have a significant impact on glycemic control. It should be noted that rosiglitazone has restricted status for use with pediatric patients in the US and Europe, so it is not yet considered a reasonable medication option for youth with T2D, despite the fact that there were relatively few adverse effects observed with its use in the trial.

The most striking finding from this study was the fact that nearly half of all youth did not achieve reasonable glycemic control despite all the attention afforded them as participants in a controlled trial. This result suggests that the majority of youth with T2D may require both oral medications and insulin fairly early in the course of their diabetes, as well as additional intervention approaches to address other relevant issues, including psychological and family functioning, and adherence, as discussed below. Failure rates were greatest in black and Hispanic youth, indicating additional treatments or culturally adapted approaches are needed for these patient populations.

While lifestyle intervention resulted in decreased BMI, this had no effect on glycemic control; more work is needed to determine what level of weight loss is needed to improve glycemic control in youth. Mean adherence to medication was reported as 84% in month eight but was only 57% at the end of the trial at month 60. The rate of attendance at lifestyle visits was 75% over two years. Only about half (54%) of participants attended 75% or more of the scheduled lifestyle intervention sessions over the course of the trial. Because the lifestyle intervention was very intensive and required frequent clinic visits with both patients and parents over the first two years, plus quarterly visits thereafter, the feasibility of this treatment approach with young patients with T2D may be limited in the clinical setting. Nevertheless, integrated behavioral and medical team management of T2D appears to offer the most effective approach for optimal management [97].

Other approaches to treatment of youth with T2D include the use of medically-supervised very low calorie diet and bariatric surgery. One report indicated that very low calorie diet for two months resulted in reduced glycosylated hemoglobin A1C and medication use in youth [98]. There is also evidence that bariatric surgery for severely obese youth with T2D may reverse diabetes and improve cardiovascular risk factors [99].

#### **Family Issues**

Family history of diabetes is very common among youth with T2D in youth [73]. Thus, many youth with T2D live with an adult family member who also has T2D, and even more have family members who are obese [88]. Many youth with T2D therefore have a shared family experience with regard to T2D, and this may have both positive and negative consequences. Several qualitative studies have addressed this issue. In one study, parents reported ambivalence about their role in their child's diabetes management: while parents acknowledged the opportunity to provide support and serve as positive role models, they also reported difficulty in setting a good example for healthy lifestyle behaviors [100]. Having family members with T2D may impact negatively on youth through family acceptance of diabetes-related health complications. When older family members have experienced impaired health due to chronic hyperglycemia such as retinopathy, nephropathy, limb amputations, and premature death, youth may perceive these

complications as an inevitable course of diabetes [101]. Parental involvement was found to be a significant correlate of glycemic control in a study of 75 youth with T2D that used a measure of family responsibilities for T2D. Results showed that youth with poor glycemic control had parents who were less involved for social and proactive care of diabetes [102].

#### Adherence Issues

There are some developmental, physical, and psychosocial features that differentiate T2D from type 1 diabetes and other chronic health conditions, and these factors may contribute to high rates of regimen non-adherence among youth with T2D. Youth with type 1 diabetes may suffer aversive consequences related to hypoglycemia and hyperglycemia if they are non-adherent. However, if youth with T2D do not take their medications or check their blood glucose, they may not experience such consequences. This perception of lack of connection between adherence and health outcomes may contribute to the high rates of non-adherence often reported in adolescents with T2D.

For example, several reports described the high rates of non-adherence to medical treatment and diet and exercise prescriptions among adolescents with T2D, noting that many patients fail to lose weight, have poor glycemic control, or drop out of treatment [103, 104, 105]. A few longitudinal studies of youth with T2D reported low follow-up rates. In a study of German and Austrian adolescents, 60% dropped out of care after a mean of 7.1 months [106], and in a study of black youth in New York, 39% of patients dropped out of medical follow-up by 2 years and 78% after 5 years [107].

T2D is usually diagnosed in early adolescence, which is a time when youth become more autonomous from their parents; thus youth with T2DM may be expected to manage their self-care tasks more independently. Furthermore, the unhealthy lifestyle habits that lead to obesity and T2D are already well established by the time of diagnosis. Parents can be responsible for physical activity and feeding of their young children, but adolescents typically have more autonomy and must be more responsible to engage in appropriate self-care behaviors on their own. In addition, for many adolescents, peer acceptance is a major issue and they may be reticent to engage in self-care behaviors that make them look different. Consequently, they may not want to check their blood glucose, eat differently, or take medication in front of their peers. The issue of non-adherence in adolescents with chronic disease can also be understood because of lack of cognitive maturity, in that most adolescents do not relate unhealthy behaviors with negative health outcomes [108].

Several qualitative studies have addressed these issues. In one study, parents reported that typical adolescent behavior such as the need for immediate gratification, affected diabetes management behaviors [100]. They also identified other factors making diabetes management difficult, including peer influences, limited awareness of long-term consequences of diabetes, family conflict, and deception. Another study examined how accurate adolescents with T2D and their parents were with regard to their overweight status [109]. Both parents and the adolescents underestimated the severity of weight issues: only 41% of parents and 35% of adolescents accurately perceived the adolescent to be overweight, while 87% were actually obese. Inaccurate perception about weight was associated with less physical activity and poorer dietary habits in the adolescents.

Adolescents' perspectives on self-management of T2D were examined in two qualitative studies. In one study, 10 African American girls were given structured interviews to identify resources and barriers for self-management [110]. Results indicated they viewed mothers and peers as sources of support, but acknowledged health comorbidities, negative peer influences, dietary and regimen challenges, and financial difficulties as barriers to effective care of T2D. Focus groups were conducted with 24 adolescents (mostly African American) with T2D in another study [111]. A number of barriers were identified including social (embarrassment, fear of rejection from peers), family (others in family who have unhealthy lifestyles or health problems from T2D), psychological (denial of health risks, not being concerned about missing medication doses, lack of normalcy), and environmental (dietary challenges at school and restaurants) barriers.

#### **Psychological Problems**

There are relatively few published studies addressing the role of psychological problems in youth with T2D. One study found that at the time of diagnosis, 20% had a pre-existing psychiatric disorder, including attention deficit disorder, depression, bipolar disorder, and schizophrenia [112]. A report from the SEARCH study found that youth with T2D, particularly boys, were significantly more likely to report depressed mood than youth with type 1 diabetes [113]. In fact, compared to boys with type 1 diabetes, boys with T2D were 3.5 times more likely to report significantly depressed mood. Twenty percent of girls and 18% of boys with T2D reported symptoms of moderate to severe depression in this study. Furthermore, poor glycemic control and more frequent emergency department visits were associated with depressed mood. A report from the TODAY study group found that 15% of youth with T2D reported significant depression, with older girls reporting more depression and depressed mood associated with lower quality of life [114]. In another report from the TODAY study group, 20% of youth reported subclinical and 6% reported clinically significant binge eating; binge eating was associated with greater obesity, more depression, and lower quality of life [115]. Reduced quality of life in youth with T2D has also been reported [116].

# Conclusions

Over the past several decades there has been a striking increase in the rate of overweight and obesity in children in the U.S, as well as in many countries throughout the world. Although the etiology of this phenomenon is multi-factorial, behavioral and environmental influences play significant roles. Similarly, rates of T2D have increased dramatically along with the rising incidence of obesity, and obesity is prominent in most cases of youth diagnosed with T2D. Children from lower income families and of ethnic minority backgrounds are at increased risk for both obesity and T2D. Obese children evidence increased metabolic risk factors, and those with a family history of T2D appear to be at greatest risk for development of T2D. Both obesity and T2D confer increased risk for development of various health disorders, contributing to the probability of decreased life expectancy. In addition, obesity and T2D in youth is associated with increased risk for psychological problems such as depression, eating disorders, and reduced quality of life, and are accompanied by unhealthy dietary and physical activity lifestyle behaviors.

Obesity and T2D thereby represent very significant public health issues in terms of both adverse personal impacts on health and costs to society through increased health care utilization over time. Efficacious treatments are available for obese children, but a major issue is how to reach the population of overweight and obese children. In-person clinical interventions involving family-based behavioral programs may be effective, but most families needing treatment for their children are unlikely to receive comprehensive evidence-based treatment programs. Internet-based programs have had some success with weight loss and maintenance and have potential for increasing the reach of effective intervention to the population. In cases of morbid obesity, inpatient and surgical approaches have been used but additional research is needed to demonstrate their safety and long-term effects. Some weight loss medications have been evaluated, but more work is needed in this area. Identification and treatment of overweight children in the school setting has some promise, as do obesity prevention programs delivered to children at school. Because treatment of obesity is only modestly effective, obesity prevention beginning in early childhood is a priority area for future research; public health and policy approaches offer promise in this regard.

The diagnosis of T2D in children and adolescence has increased significantly in the past two decades in the U.S. and is also increasing in prevalence throughout the world, particularly among certain ethnic minority populations. Research indicates that youth with T2D are likely to develop serious diabetes-related health complications relatively early in adulthood, contributing to decreased life expectancy. Even in youth with T2D, early signs of microvascular and macrovascular health complications may be present. Family history of T2D in very common among youth with T2D, and research suggests family factors are significant influences on youths' T2D management. For example, family members with high risk behavioral lifestyles may not provide good models for healthy dietary intake and physical activity. Not surprisingly, youth with T2D are likely to have unhealthy dietary and physical activity lifestyle habits.

Psychological factors also play an important role in T2D management, as studies show such youth are at risk for depression, binge eating, and reduced quality of life. Physicians report major challenges in clinical care of T2D in youth, including high risk behavioral lifestyles, psychological problems, reduced patient motivation, and cultural barriers. Consensus guidelines exist for the treatment of T2D in youth, emphasizing the importance of integrated interdisciplinary team care including behavioral health specialists. However, recent research indicates that most youth with T2D do not attain optimal glycemic control, remain overweight, and often do not stay in medical treatment. National and international organizations such as the American Diabetes Association and the International Society of Pediatric and Adolescent Diabetes recommend that physicians, nurses, dieticians, and mental and behavioral health professionals collaborate on interdisciplinary teams to effectively help youth with T2D.

Given the fact that youth with T2D are at high risk for development of diabetes-related health complications, identification of effective medical and behavioral treatment approaches remains a priority. More research is needed better understand how psychological and psychosocial factors affect regimen adherence, including medication taking and blood

glucose monitoring, as well as weight loss efforts, attendance at follow-up outpatient visits, as well as glycemic control. More studies should also address the treatment of psychological disorders in order to improve diabetes management and quality of life.

Given the substantial health risks associated with poor control of T2D in youth, programs should screen high-risk children, including overweight, ethnic minority youth with a family history of T2D. Evidence-based weight control treatments that may reduce T2D risk should focus on these high-risk children. Research focusing on the prevention of T2D in children and adolescents continues to be a high priority for public health.

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