Addressing Prediabetes in Childhood Obesity Treatment Programs: Support from Research and Current Practice

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Abstract

Background: Type 2 diabetes mellitus (T2DM) and prediabetes have increased in prevalence among overweight and obese children, with significant implications for long-term health. There is little published evidence on the best approaches to care of prediabetes among overweight youth or the current practices used across pediatric weight management programs.

Methods: This article reviews the literature and summarizes current practices for screening, diagnosis, and treatment of prediabetes at childhood obesity treatment centers. Findings regarding current practice were based on responses to an online survey from 28 pediatric weight management programs at 25 children’s hospitals in 2012. Based on the literature reviewed, and empirical data, consensus support statements on prediabetes care and T2DM prevention were developed among representatives of these 25 children’s hospitals’ obesity clinics.

Results: The evidence reviewed demonstrates that current T2DM and prediabetes diagnostic parameters are derived from adult-based studies with little understanding of clinical outcomes among youth. Very limited evidence exists on preventing progression of prediabetes. Some evidence suggests that a significant proportion of obese youth with prediabetes will revert to normoglycemia without pharmacological management. Evidence supports lifestyle modification for children with prediabetes, but further study of specific lifestyle changes and pharmacological treatments is needed.

Conclusion: Evidence to guide management of prediabetes in children is limited. Current practice patterns of pediatric weight management programs show areas of variability in practice, reflecting the limited evidence base. More research is needed to guide clinical care for overweight youth with prediabetes.

Introduction

The increased prevalence of obesity, particularly severe obesity, in all pediatric age groups, has been accompanied by an increase in type 2 diabetes mellitus (T2DM), prediabetes, and insulin resistance (IR).1–4 Along with other comorbidities of obesity, including hypertension, dyslipidemia, fatty liver disease, musculoskeletal disorders, and cardiovascular disease, T2DM and its complications represent a significant cause of long-term disability within the US population and a challenge to the resources of the US healthcare system.5–7 Still, little evidence exists in pediatric populations for effective prevention and treatment of T2DM.2,5,8 Currently, it is estimated that one third of US youth are overweight or obese, and up to 15% of adolescents may have prediabetes and/or diabetes.1

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Adolescents and young adults with T2DM are expected to lose 15 years from their life expectancy and may experience severe, chronic complications by their forties.7,9-11 Most diagnostic tools and therapeutic interventions currently in use for pediatric T2DM are based on information extrapolated from adult literature. However, the pathophysiology and response to treatment varies between children and adults. The TODAY study, the first long-term study of children with T2DM, and others have reported faster progression of T2DM and beta-cell failure in children, compared to adults, and poor treatment results.12-15

Data collected from 2001 through 2005 as part of the SEARCH study,16 a large, multi-center study of physician-diagnosed diabetes among youth 0–19 years of age, provide estimates of prevalence and incidence rates of T2DM by age and ethnicity. The prevalence of T2DM in 2001 was lowest among non-Hispanic white youths 10–19 years of age at 0.18 in 1000, with an incidence of 3.7 per 100,000 person-years during the 4-year study.17 Prevalence and incidence rates were higher among African American (1.06 in 1000; 19.0 per 100,000 person-years), Hispanic (0.46, 11.6), and Asian/Pacific Island youth (0.52, 12.1) than non-Hispanic white youth, with the highest rates among Navajo youth (1.45; 27.7).18-21

The impetus to complete this survey of current practice and review of current evidence stems from the high prevalence of childhood and adolescent obesity, increasing diagnosis of prediabetes and T2DM, and interest in earlier identification and prevention.22,23 The primary aims of the article are to identify practices supported by evidence and report consensus of current practice among childhood obesity specialists for two areas: (1) screening of obese children and adolescents for prediabetes and T2DM and (2) prevention of progression from prediabetes to T2DM. This article describes the practices of medical weight management clinics, but is also relevant to primary care providers who either manage obese children collaboratively with weight management programs or those who must address these issues without access to outpatient tertiary care weight management.2,24 The article also highlights subsets of the pediatric population identified as having unique needs or differences with respect to the diagnosis and management of prediabetes, such as specific age groups,25 racial/ethnic groups,2,9,10 and patients with co-occurring conditions or treatments (e.g., antipsychotics).

Methods

The clinical practices that are included in this literature review and survey were identified by consensus of the Medical Management Committee of the FOCUS on a Fitter Future (FFF) Group, sponsored by the Children’s Hospital Association (CHA). Over 5 years (2008–2013), the FFF group of over 100 representatives from 28 weight management programs at children’s hospitals across the United States met in person quarterly and by telephone weekly to monthly.26 Each institution self-selected to participate in FFF by an application process available to 250 member institutions of the CHA. The FFF group was unique during this time period as a multidisciplinary longitudinal working group of clinical experts and researchers focusing on the treatment of childhood obesity, particularly severe obesity.

Components of practice were included in this survey and review because the committee judged each to raise relevant clinical questions, have uncertain evidence support, and/or be potential sources of variation in care. Current practices are reported from a survey of 28 pediatric weight management programs at 25 children’s hospitals with wide geographic distribution across the United States. The survey was completed by at least one provider from each of the sites participating in the FFF group in 2012. Three hospitals had more than one obesity clinic or program employing different clinical approaches and therefore completed a survey for each program to capture practice variation.

The interprofessional Medical Management Committee from FFF (the Committee) rated the quality of available evidence and determined the strength of support for each practice using a framework described by the American Academy of Pediatrics (AAP) Steering Committee on Quality Improvement and Management.27 The quality of evidence supporting each practice was assigned as: A. Well-designed randomized, controlled trials (RCTs) or diagnostic studies on relevant populations, B. RCTs with minor limitations or overwhelmingly consistent observational studies, C. Observational studies, or D. Expert opinion. The quality of evidence and the balance of benefits and harms for each practice were weighed to arrive at a consensus statement within the following categories: strong support for the practice; support for the practice; an option to consider the practice; no position; or a do not support statement for the practice. Conclusions of the Committee were presented at a meeting of the entire FFF group, from which feedback was incorporated. The revised statements were approved by the entire FFF group as consensus statements. Members of the following disciplines were involved in the review process: pediatricians, pediatric endocrinologists, dietitians, psychologists, social workers, exercise physiologists, and physical therapists. The group identified opportunities for further research based on evidence reviewed and variations within current practice.

Results

Identification of Risk

The American Diabetes Association (ADA) Expert Committee on the Diagnosis and Classification of Diabetes Mellitus first recognized prediabetes in 1997.28 Prediabetes can be defined by abnormal glucose regulation, including impaired fasting glucose and/or impaired glucose tolerance (IGT) and/or glycated hemoglobin (A1c). Data from adult and adolescent studies have shown that prediabetes, particularly in those with an elevated BMI, significantly increases the risk of developing diabetes, but is reversible.29

In one study, up to 50% of severely obese adolescents with prediabetes returned to normal glucose tolerance over
20 months, whereas 24% showed progression from prediabetes to diabetes, and those with the highest BMI had the highest risk of disease progression. Another study showed that 75% of obese white teens with IGT returned to normal glucose metabolism, whereas 2% progressed to diabetes. Based largely on data from the Diabetes Prevention Program (DPP) Research Group study showing successful delay or prevention of onset of T2DM in adults, there is mounting interest in early detection of prediabetes in childhood.

Clinical screening. Medical providers who routinely carry out laboratory screening of obese children, as recommended by professional societies, are likely to identify some children with blood glucose or A1c measurements in the prediabetes range. Table 1 summarizes recommendations for T2DM screening adapted from the 2007 Expert Committee Recommendations Regarding the Prevention, Assessment, and Treatment of Child and Adolescent Overweight and Obesity.

Special at-risk populations. In addition to obesity, multiple factors add to diabetes risk and warrant consideration. Genetic and environmental risk factors include female gender, sedentary behavior, and family history of T2DM. Female adolescents are 1.7 times more likely than boys to develop T2DM. At least 74% of children with T2DM have a first- or second-degree relative with the disorder. Risk is increased if a parent develops T2DM before age 30. Prenatal nutrition and intrauterine environment affect risk; low and high birth weight and maternal gestational diabetes or T2DM are the greatest risk factors. Ethnic minorities are at higher risk, including African Americans, Hispanics, and Native Americans. Finally, fat distribution plays a role; children who have central obesity with higher visceral or abdominal fat stores are at higher risk for IR and progression to diabetes.

Patients prescribed second-generation antipsychotics (SGAPs) are another group at increased risk for weight gain and secondary diabetes. Among adults with schizophrenia and affective disorders taking SGAPs, the prevalence of diabetes is estimated at 1.5–2.0 times that of the general population. The pediatric literature is limited; however, one retrospective chart review estimated a 4-fold increased incidence of diabetes among SGAP-exposed pediatric patients, compared to nonpsychotropic medication users. An observational study of metabolic effects of SGAP therapy in children found an average weight gain of 8.5 kg in 11 weeks.

Clinical practice by children’s hospital-based weight management clinics in screening for prediabetes and type 2 diabetes mellitus. All respondents, representing 28 programs at 25 children’s hospitals, indicated that they screen patients for prediabetes and T2DM. Twenty-five clinics reported the criteria used to target screening. The majority (n = 18 of 25; 72%) used BMI as a criterion; however, cutoff points varied among programs (four screen for BMI ≥95th percentile, three for ≥85th percentile, one for >40 kg/m², and one for ≥99th percentile or ≥95th percentile with comorbidities). Seven sites screen all referred patients. Additional factors used to target screening included acanthosis nigricans (n = 4), family history of T2DM (n = 2), age (n = 3), and clinical signs of diabetes (n = 1).

Consensus statement of Focus on a Fitter Future on clinical screening. Overweight children with cardiometabolic comorbidity and obese children should be screened periodically for prediabetes and T2DM after age 10 years or after onset of puberty (Evidence D). Early identification of prediabetic or diabetic state may prevent progression of disease or facilitate disease management. Additional study of the predictive value of abnormal blood glucose measures for the development of T2DM in children is needed.

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Table 1. Type 2 Diabetes Screening in Asymptomatic Pediatric Patients

<table>
<thead>
<tr>
<th>BMI criteria for screening</th>
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</thead>
<tbody>
<tr>
<td>1. All children or adolescents who are severely obese (BMI &gt; 99th percentile)</td>
</tr>
<tr>
<td>2. Children or adolescents at the earlier age of 10 or onset of puberty</td>
</tr>
<tr>
<td>a) Obesity (BMI ≥ 95th percentile)</td>
</tr>
<tr>
<td>b) Overweight (BMI 85th–&lt; 95th percentile) with one or more additional risk factors</td>
</tr>
<tr>
<td>Risk factors</td>
</tr>
<tr>
<td>- Family history of T2DM in first- or second-degree relative</td>
</tr>
<tr>
<td>- High-risk race/ethnicity (African American, Latino, Native American, Asian American, or Pacific Islander)</td>
</tr>
<tr>
<td>- Signs of insulin resistance or conditions associated with insulin resistance (hypertension [systolic or diastolic blood pressure &gt; 95th percentile for age and sex], dyslipidemia, polycystic ovary syndrome, acanthosis nigricans, or small for gestational age at birth)</td>
</tr>
<tr>
<td>- Maternal history of diabetes or gestational diabetes during the child’s gestation, low or high birth weight</td>
</tr>
<tr>
<td>- Patients prescribed SGAPs</td>
</tr>
<tr>
<td>Age at initial testing</td>
</tr>
<tr>
<td>- 10 years or at onset of puberty if puberty occurs at a younger age</td>
</tr>
<tr>
<td>- Under age 10, or prepubertal if child has BMI &gt; 99th percentile or has one or more additional risk factors</td>
</tr>
<tr>
<td>Retesting</td>
</tr>
<tr>
<td>- Biannually if normal, more frequently for abnormal values, rapid increases in weight, development of other comorbidities (hypertension or dyslipidemia), and/or onset of puberty</td>
</tr>
</tbody>
</table>

*Adapted from 2007 Expert Committee Recommendations Regarding the Prevention, Assessment, and Treatment of Child and Adolescent Overweight and Obesity.
Laboratory Screening and Diagnostic Tests

Tests recommended by the ADA for screening and diagnosing prediabetes and diabetes include fasting plasma glucose (FPG), A1c, and a 2-hour oral glucose tolerance test (OGTT). Test selection for individual patients may vary based on the clinical findings, risk factors, and resources available. Relative advantages of fasting glucose and A1c as screening tests are listed in Table 2 and diagnostic cutoffs are listed in Table 3. An analysis of laboratory data from 1156 overweight and obese adolescents from the National Health and Nutrition Examination Survey 1999–2006 found that an A1c cutoff of 6.5% was 75% sensitive for identifying diabetes, compared to a single FPG, though this study was limited by a very low number of undiagnosed diabetics (n = 4) and the possibility of erroneous reports of fasting. The same study found that, for adolescents compared to adults, A1c was a significantly worse predictor of prediabetes defined by FPG (area under the receiver operating curve, 0.61 vs. 0.74; p < 0.01). A recent position statement from the Pediatric Endocrine Society notes that the diabetes diagnostic criteria are based on long-term health outcomes assessed in adults, but have not been validated in pediatric populations.

Indices of insulin resistance. Accurate testing of IR is labor intensive, invasive, and expensive (i.e., the hyperinsulinemic-euglycemic and hyperglycemic clamp techniques). Therefore, several indices have been developed and studied, such as the homeostatic model assessment of insulin resistance (HOMA-IR), the quantitative insulin sensitivity check index, the continuous infusion of glucose with model assessment, and the Matsuda index. The most widely used and studied is HOMA-IR. No known international standards for abnormal levels currently exist for these indices in children, the assay itself is not standardized, and studies have shown that insulin indices do not substantially change predictive value for diabetes beyond other more-routine measures. The findings of these studies highlight the concern that insulin levels may be a poor predictor of diabetes risk because, whereas IR may be accompanied by high insulin levels initially, insulin secretion may decrease later in the progression toward diabetes as a result of glucotoxicity and beta-cell failure.

Clinical practice findings for screening tests used to screen for prediabetes. All 28 respondents reported screening for prediabetes, using a variety of test combinations. The most widely used tests were A1c (n = 23) and FPG (n = 22), with OGTT used less often (n = 10). Three clinics used A1c alone, five used fasting glucose alone, 14 used fasting glucose plus A1c, and six used all three tests for initial screening. Most respondents repeated normal laboratory tests either in 12 months (n = 9) or between 6 and 12 months (n = 9). Some respondents repeated normal labs sooner, at 3–6 months (n = 5) and later at 12–24 months (n = 2). For abnormal laboratory tests, most repeated tests at either 3–6 (n = 9) or 6–12 months (n = 8). A few (n = 3) repeated screening on an as-needed basis.

Clinical practice findings for screening insulin resistance. All respondents reported screening for IR by assessing for acanthosis nigricans or physical examination. Twenty-five of 25 (88%) respondents screened for IR using fasting insulin or a ratio of fasting glucose to insulin. There was marked variability in the criteria used to identify children to be screened: Thirteen clinics (52%) screened all children who were referred for weight management. Of the remaining 12 clinics, four used BMI percentile criteria only (two >95th and two >99th), six used the presence of acanthosis nigricans and a BMI cutoff (one >85th percentile with risk factors and five >95th percentile), and

### Table 2. Comparison of Tests To Screen for Prediabetes

<table>
<thead>
<tr>
<th>Fasting plasma glucose</th>
<th>Hemoglobin A1c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Higher sensitivity compared to A1c in adult populations (in adults up to one third more diagnosed)</td>
<td>Fasting is not required.</td>
</tr>
<tr>
<td>Unaffected by conditions associated with high red blood cell turnover (e.g., anemia, blood transfusion, pregnancy)</td>
<td>Low intradividual variability</td>
</tr>
<tr>
<td>Less expensive and more convenient compared to OGTT</td>
<td>Less day-to-day variability with illness or stress</td>
</tr>
<tr>
<td>Low reproducibility</td>
<td>Reflects glycemic levels for the past 3 months</td>
</tr>
<tr>
<td>OGTT, oral glucose tolerance test; A1c, glycosylated hemoglobin.</td>
<td>Good predictor of diabetes-related complications in adults</td>
</tr>
</tbody>
</table>

### Table 3. Summary of Criteria for Diagnosing Prediabetes and Diabetes

<table>
<thead>
<tr>
<th></th>
<th>Prediabetes</th>
<th>Diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fasting plasma glucose&lt;sup&gt;a&lt;/sup&gt;</td>
<td>100–125 mg/dL</td>
<td>≥126 mg/dL</td>
</tr>
<tr>
<td>2-hour plasma glucose (OGTT)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>140–199 mg/dL</td>
<td>≥200 mg/dL</td>
</tr>
<tr>
<td>Random plasma glucose&lt;sup&gt;c&lt;/sup&gt;</td>
<td>Not applicable</td>
<td>≥200 mg/dL</td>
</tr>
<tr>
<td>Hemoglobin A1c</td>
<td>5.7–6.4%</td>
<td>≥6.5%</td>
</tr>
</tbody>
</table>

Adapted from the American Diabetes Association Recommendations.<sup>50</sup>

<sup>a</sup>Fasting for at least 8 hours with no calorie intake.

<sup>b</sup>OGTT using a load 1.75 g/kg of body weight of glucose with a maximum of 75 g.

<sup>c</sup>In patients with hyperglycemic crises or classic symptoms of hyperglycemia (e.g., polyuria, polydipsia).

<sup>d</sup>In the absence of unequivocal hyperglycemia, diagnosis is confirmed if two different tests are above threshold or a single test is above threshold twice.

OGTT, oral glucose tolerance test; A1c, glycosylated hemoglobin.
two used a cutoff based on onset of puberty and BMI >85th percentile. Additional screening factors used included family history of T2DM (n=3) and ethnicity (n=1). Three clinics choosing not to screen for insulin levels reported the following reasons: Data did not change management, desire to conserve financial resources, and advice from endocrinologists at the institution who recommended screening for abnormal blood glucose measures only.

Testing can be considered in younger children with severe obesity or children prescribed SGAPs. The authors do not support laboratory screening for fasting insulin in obese patients because current evidence does not indicate changes to treatment based on results, and insulin levels may be low as patients lose insulin secretory ability. Thus, low insulin levels may represent worsening of beta-cell status, rather than improvement in IR (Evidence D).

Further study is needed of the predictive value of laboratory markers of blood glucose and IR over time for progression to T2DM, especially in severely obese children and other groups expected to be at highest risk.

Type 2 Diabetes Prevention

Halting the progression toward T2DM, both from normal glucose regulation to prediabetes and from prediabetes to diabetes, is one of the key goals of obesity management. Several studies have shown that lifestyle change consisting of physical activity, lower daily energy intake, and modest weight reduction can reduce T2DM incidence in adults at high risk for diabetes. The progression to T2DM typically occurs in individuals who are overweight or obese and sedentary. Resistance to the action of insulin in liver and skeletal muscle can lead to hyperinsulinemia, often marked by the presence of acanthosis nigricans, especially in more darkly pigmented individuals. Pancreatic beta cells may eventually fatigue as IR worsens, and waning insulin secretion leads to moderate glucose excursions in prediabetes. More-advanced beta-cell failure, in the presence of persistent IR, results in overt T2DM as glucose toxicity further impairs insulin secretion and leads blood glucose to rise uncontrollably. Intensifying interventions early in the disease course, with the goals of glucose normalization and preservation of pancreatic beta-cell function, seems to offer the best chance for preventing the development of diabetes or slowing the progression to diabetes. While new cases of T2DM occurred in the intervention arms of the DPP over time, the incidence of T2DM remained below that of the control group. Thus, the ADA’s Professional Practice Committee recommends that adults with prediabetes be referred to a program targeting weight loss of 7% and increasing moderate physical activity to >150 minutes per week based on data from the DPP. Studies in adolescents have also demonstrated an increase in insulin sensitivity with diet and exercise-induced weight loss and resolution of prediabetes in multicompartment lifestyle programs.

Role of medication in diabetes prevention. IR precedes development of T2DM, which occurs when pancreatic beta cells fail to compensate for IR. Several large RCTs of pharmacological interventions to decrease the incidence of new-onset T2DM have been conducted in adults with mixed results. Metformin, a biguanide, decreases hepatic glucose production and also increases insulin sensitivity in peripheral tissues. In the DPP trial, metformin, at a dose of 850 mg twice-daily, showed a 31% reduction in risk, compared to placebo, over 2.8 years (compared to a 58% reduction in the lifestyle group). A meta-analysis from five randomized clinical trials of adults on metformin found a 40% decline in progression to type 2 diabetes among those at risk. In obese adolescents, a meta-analysis including three small, short-term randomized trials of metformin with IR found a reduction in BMI and fasting insulin with treatment. Three other small randomized trials in normoglycemic obese children with elevated fasting insulin showed reduction in fasting glucose and insulin. However, none of these studies lasted longer than 6 months.

Clinical practice findings for use of metformin in prediabetes. Among children’s hospital obesity programs, 14 of 28 respondents (50%) indicated that they use metformin to treat prediabetes, and the doses prescribed ranged from 500 to 2000 mg per day. Seven of these 14 clinics treating prediabetes with metformin reported systematically tracking patient results, including BMI and laboratory values. Eight respondents reported using laboratory triggers for referral to endocrinology: elevated fasting glucose >100 mg/dL (n=4), abnormal OGTT (n=3), and A1c >5.7% (n=1). Reasons for stopping metformin included improvement in blood glucose (n=5), decrease in BMI of 2 kg/m² (n=1), and improvement in insulin (n=1). Three respondents indicated that an endocrinologist was routinely consulted regarding the decision to stop metformin.

Clinical practice findings for use of metformin in insulin resistance. In addition to the use of metformin for prediabetes, 11 programs reported prescribing metformin for elevated fasting insulin or HOMA-IR in the absence of abnormal blood sugar or polycystic ovary syndrome.
Role of nutrition in diabetes prevention. Support for healthy nutrition is essential for management and prevention of diabetes. Medical nutrition therapy with a registered dietitian provides specialized support in treating youth with prediabetes and T2DM. Of note, studies of dietary interventions reviewed below have employed registered dietitians to design and deliver the nutrition interventions. Weight loss of 5–7% is the standard recommendation for diabetes prevention in adults based on the DPP, which used a low-fat diet to decrease calorie intake. Research studies to inform similar recommendations in youth are needed, especially during critical periods of increased IR, such as puberty. Studies suggest that lifestyle intervention in children also leads to metabolic improvement.

Although there is no prescribed diet for diabetes prevention in youth, research on low glycemic diets among adults and youth demonstrate improvement in insulin secretion and body composition without evidence of harm. A low glycemic index (GI) diet generally refers to a balanced diet with carbohydrate content primarily from low to medium glycemic load foods (those that produce less-rapid rise in blood glucose and have lower overall carbohydrate content). The most common high GI foods include processed grains (white bread and white rice) and added sugars of all types. In two studies comparing low and high GI diets in 38 youth with obesity and T2DM or prediabetes, the low GI diet had significantly greater reductions in IR. Additional research found a low GI diet decreased adipose tissue more than low-kilocalorie and low-fat diets and increased high-density lipoprotein cholesterol and satiety. An RCT comparing low versus high glycemic load hypocaloric diets for 6 months found greater reductions in waist circumference, BMI z-score, and HOMA-IR with the low GI diet.

In children who are severely obese, few studies examined the safety and effectiveness of rapid weight loss diets. A study of 46 adolescents randomized to a low-calorie, low-fat diet or a very-low-carbohydrate (20 g/day) diet demonstrated safety and efficacy of the very-low-carbohydrate diet. Another study comparing 58 children randomized to either a very-low-carbohydrate ketogenic diet or a hypocaloric diet for 6 months found greater improvements with the ketogenic diet in weight, fat mass, waist circumference, fasting insulin, and HOMA-IR. Larger and longer-term studies of very-low-carbohydrate diets for severely obese children with prediabetes are needed.

Role of exercise in diabetes prevention. Exercise, combined with healthful dietary changes using a behavioral approach, is a key therapeutic recommendation for obesity reduction and T2DM prevention. In studies of adults, exercise increases insulin sensitivity within 1 week of an intervention, lasting for 3–4 days after exercising. In obese children, exercise alone has been shown to improve IR even without changes in body weight or body composition. A variety of exercise interventions have been tested, including 1-hour circuit training sessions three times per week, sports activities for 20–45 minutes three times per week, and progressive resistance training. Individual differences in physiological changes with exercise depend on baseline fitness, genetic effects, and lifestyle.

Role of behavioral health professionals in diabetes prevention. Standard practice for treating childhood obesity in multidisciplinary referral settings includes behavioral health services delivered by a doctoral-level pediatric psychologist, if possible. There is emerging literature underscoring the benefits of including a behavioral health specialist in treating T2DM. Earlier involvement of behavioral health professionals for those with prediabetes may help prevent disease progression. As in treating obesity, targeting behavioral treatment to the family unit of youth with prediabetes or T2DM may be especially important, given high rates of T2DM and problematic behaviors among family members.

In addition to facilitating family-based lifestyle behavior change, psychologists can address comorbid psychopathology that contributes to disease progression or hinders treatment. Emotional and behavioral difficulties represent barriers to adherence with pediatric medical regimens in
general. Almost 1 in 5 youth with newly diagnosed T2DM may have pre-existing psychiatric diagnoses. Researchers have found that the progression of IR during childhood and adolescence is predicted by depressive symptomatology at baseline, independent of BMI. Psychologists also can be instrumental in addressing other adherence barriers, such as family conflict and poor time management.

Psychologists can aid a multidisciplinary team in providing culturally effective pediatric healthcare. Children and adolescents from low socioeconomic backgrounds, ethnic minority groups, and single-parent families tend to have more problems with adherence to complex chronic disease regimens. In general, racial and ethnic minorities utilize mental health services at lower rates than non-Latino whites. Therefore, pediatric psychologists working with children and adolescents with prediabetes should be sensitive to cultural issues and tailor their interventions for each family.

Referral to Endocrinology/Diabetes Specialists

The ADA recommendations state that children meeting criteria for T2DM are to be referred to endocrine specialists to confirm diagnosis and discuss decisions about medication and how to manage comorbidities. An endocrinologist should be consulted to distinguish between type 1 and 2 diabetes. The AAP recommends that weight management specialists co-manage T2DM with a pediatric endocrinologist. A primary care professional (pediatrician, family practitioner, or internist) who has expertise in diabetes management may serve as a consultant in the absence of an available pediatric endocrinologist.

Clinical practice findings for co-management with an endocrinologist. Whereas some pediatric obesity clinics are directed by an endocrinologist, others have more-limited access to endocrinologists. Almost all of the children’s hospital obesity clinics in our survey ($n = 23$ of $25$; $92\%)$ do not include endocrinologists on the weight management team; all of these refer patients with T2DM to endocrinology, primarily for medication management. The majority of respondents ($n = 16$ of $22$; $72\%)$ indicated that they do not refer patients with prediabetes to endocrinologists.

Consensus statement of Focus on a Fitter Future on co-management of T2DM with an endocrinologist. Consistent with AAP recommendations the Committee supports that weight management specialists co-manage T2DM with a pediatric endocrinologist (Evidence D).

Conclusion

Given the increased prevalence of prediabetes and T2DM among children, guidance regarding screening and management of prediabetes is needed to ensure best clinical outcomes and reduce healthcare costs. However, data to guide T2DM prevention in children are limited. This article summarizes the current literature on screening and diagnosis of prediabetes and the prevention of T2DM among overweight youth. Variability in practices in assessment and treatment of IR and prediabetes may be attributed to the lack of high-quality evidence and limited availability of pediatric endocrinology expertise. Based on the best available evidence, our experience in treating obese children, and consideration of possible harms and benefits, the authors offer statements of support reflecting consensus of the FFF Medical Management Committee with consideration of the level of evidence, uniformity of current practice, potential costs, and benefits for practices that were reviewed (Table 4). Further research is needed to guide which therapies might best prevent progression of prediabetes to T2DM and which children should be targeted. In order to answer important clinical and public health questions, large-scale, multi-center studies of interventions to reduce the risk of T2DM are needed. A multi-center research network of childhood obesity treatment programs, working collaboratively with multidisciplinary teams including pediatric endocrinologists, could provide the platform required to answer many of these questions.

Acknowledgments

Between 2008 and 2013, CHA (formerly known as NACHRI, the National Association of Children’s Hospitals and Related Institutions) convened FFF to articulate the role of children’s hospitals in combating pediatric obesity while building consensus on performance measurement and quality improvement. FFF examined the state of care for obese children and adolescents and continues to communicate the best ways to ensure their physical well-being and emotional safety. FFF was guided by multidisciplinary teams representing more than a dozen pediatric healthcare professions—physicians of several specialties, dietitians, exercise specialists, nurses, physical therapists, obesity program managers, psychologists, and social workers—involved with childhood obesity. This article represents the work of the Medical Treatment Committee in consensus with the entire FFF group. FFF was funded, in part, by the Mattel Children’s Foundation. Dr. Haemer was supported by the Children’s Hospital Colorado Research Institute Research Scholar Award. Dr. Rhodes was supported by the New Balance Foundation Obesity Prevention Center Boston Children’s Hospital.

Author Disclosure Statement

CHA (the Association) was the project sponsor. The sponsor facilitated collection of data and hosted study.
<table>
<thead>
<tr>
<th>Practice</th>
<th>Evidence quality</th>
<th>Balance of benefits to harms</th>
<th>Current practice in obesity treatment programs</th>
<th>Support for practice</th>
<th>Comments on need for further study</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overweight children with cardiometabolic comorbidity and obese children should be screened for prediabetes or type 2 diabetes after age 10 years or after onset of puberty.</td>
<td>D - Treatment of obesity in children with prediabetes or insulin resistance results in improvement of prediabetes and/or insulin resistance, but no study has examined prevention of progression to T2DM in children. Consistent with Expert Committee Recommendations.</td>
<td>Benefits outweigh harms - Harms: Financial cost, test-related anxiety, risk of false positives - Benefits: The benefit of lifestyle intervention for prediabetes in adults is documented; the benefit of screening and preventive treatment is not as well known in adolescents. Programs may target limited weight management resources to those at highest risk.</td>
<td>Consistent: Testing was reported by all centers. Varied: Centers varied with regard to screening criteria by BMI status, age, and other risk factors.</td>
<td>Support - Large, prospective trials are needed to determine the effect of weight management treatment for prevention of progression from prediabetes to T2DM. Additional study is needed testing the effectiveness of treatment for T2DM that is identified early through targeted screening.</td>
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<tr>
<td>Fasting plasma glucose, hemoglobin A1c (A1c), and OGTT can be used to screen for prediabetes in children presenting to tertiary weight management programs.</td>
<td>B - Studies support use of these tests in making a diagnosis, but they are limited by small sample sizes or extrapolation from studies in adults. Test cutoffs are not as well validated in children, especially for prediabetes.</td>
<td>Benefits outweigh harms - Harms: Financial cost and risk of false positives/ negatives - Benefits: Sensitivity, specificity, cost, and convenience vary by test (see Table 2).</td>
<td>Consistent: Most centers use both A1c and fasting glucose. Varied: Varied BMI and age cutoffs are used to initiate screening; follow-up testing protocols also vary in frequency and choice of test.</td>
<td>Support - Recognizing the clinician’s option to select from one or more of the available tests Further research is needed to define the testing protocol with maximum sensitivity and specificity at lowest relative cost.</td>
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<tr>
<td>Testing for insulin resistance using fasting insulin and/or HOMA-IR</td>
<td>D - Evidence is lacking about the benefits of using insulin screening.</td>
<td>Harms outweigh benefits - Harms: Financial cost, lack of standardization in laboratory measures - Benefits: Unknown; there is a lack of evidence to support changes in management based on insulin level; low insulin can reflect either improved insulin resistance or beta cell failure.</td>
<td>Varied: Majority of programs tested insulin, but based on variable criteria of BMI and comorbidity. Some centers have collected this as part of a research study and a few use this as a criteria to treat with metformin.</td>
<td>Do not support - Further study is needed to determine the value of laboratory measurement of insulin for prognosis or targeting of interventions. Costs currently outweigh lack of known benefit.</td>
<td></td>
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continued on page 300
<table>
<thead>
<tr>
<th>Practice</th>
<th>Support Level</th>
<th>Evidence</th>
<th>Benefits</th>
<th>Harms</th>
<th>Support</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of metformin to prevent progression of prediabetes to T2DM</td>
<td>C</td>
<td>Metformin is less effective than intensive lifestyle management in adults. Consistent observational evidence shows reversion to normoglycemia in a high proportion of prediabetic youth without medication.</td>
<td>Unclear</td>
<td>Harms: Medication cost given the prevalence of prediabetes is relatively high; short- and long-term adverse effects. Benefits: Unknown because T2DM prevalence is low and effect of metformin on prevention of T2DM in prediabetic children is unknown.</td>
<td>Varied: More than one third of programs (39%) prescribe metformin.</td>
<td>No position</td>
</tr>
<tr>
<td>Low glycemic index diet to treat prediabetes in obese youth</td>
<td>B</td>
<td>Small, high-quality studies consistently show metabolic improvement with low glycemic load diets.</td>
<td>Benefits outweigh harms</td>
<td>Harms: Cost of dietary instruction, financial costs to families associated with changing diets</td>
<td>Benefits: Metabolic improvement, potential weight loss</td>
<td>Not reported</td>
</tr>
<tr>
<td>Increased moderate-to-vigorous activity to treat prediabetes in obese youth</td>
<td>B</td>
<td>Physical activity is consistently correlated with better glucose regulation in obese children, independent of weight loss.</td>
<td>Clear preponderance of benefits over harms</td>
<td>Harms: Risk of injury, time required for exercise</td>
<td>Benefits: Metabolic improvement, potential weight loss, other health advantages of exercise</td>
<td>Not reported</td>
</tr>
<tr>
<td>Pediatric psychologists, or other behavioral health specialists, should be included on teams treating children with prediabetes or diabetes.</td>
<td>C</td>
<td>High rates of psychological comorbidity exist among children with prediabetes/diabetes. Behavior change is the mainstay of effective weight management, with evidence to support its effectiveness.</td>
<td>Clear preponderance of benefits over harms</td>
<td>Harms: Cost</td>
<td>Benefits: May improve weight outcomes, address psychopathology</td>
<td>Not reported</td>
</tr>
<tr>
<td>Weight management specialists co-manage T2DM with a pediatric endocrinologist</td>
<td>D</td>
<td>This practice is recommended by the AAP clinical practice guideline: “Management of Newly Diagnosed Type 2 Diabetes Mellitus (T2DM) in Children and Adolescents.”¹⁰⁸</td>
<td>Benefits outweigh harms</td>
<td>Harms: Cost</td>
<td>Benefits: Expertise in medication management and surveillance for medications that are used infrequently by general pediatricians</td>
<td>Consistent: Weight management programs that do not include endocrinologists typically refer for T2DM, but not prediabetes</td>
</tr>
</tbody>
</table>

HOMA-IR, homeostatic model assessment for insulin resistance; T2DM, type 2 diabetes mellitus; A1c, glycosylated hemoglobin; OGTT, oral glucose tolerance test; AAP, American Academy of Pediatrics.
group meetings, but was not involved in the data analysis or the decision to submit the manuscript for publication. The views expressed are those of the authors and do not necessarily reflect those of the Association. Dr. Rhodes reports receiving research funding from Merck, and her spouse owns stock in Bristol-Myers Squibb. The remaining authors have no disclosures.

References


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