



CLINICAL PRACTICE GUIDELINE

Management of Newly Diagnosed Type 2 Diabetes Mellitus (T2DM) in Children and Adolescents

abstract

FREE

Over the past 3 decades, the prevalence of childhood obesity has increased dramatically in North America, ushering in a variety of health problems, including type 2 diabetes mellitus (T2DM), which previously was not typically seen until much later in life. The rapid emergence of childhood T2DM poses challenges to many physicians who find themselves generally ill-equipped to treat adult diseases encountered in children. This clinical practice guideline was developed to provide evidence-based recommendations on managing 10- to 18-year-old patients in whom T2DM has been diagnosed. The American Academy of Pediatrics (AAP) convened a Subcommittee on Management of T2DM in Children and Adolescents with the support of the American Diabetes Association, the Pediatric Endocrine Society, the American Academy of Family Physicians, and the Academy of Nutrition and Dietetics (formerly the American Dietetic Association). These groups collaborated to develop an evidence report that served as a major source of information for these practice guideline recommendations. The guideline emphasizes the use of management modalities that have been shown to affect clinical outcomes in this pediatric population. Recommendations are made for situations in which either insulin or metformin is the preferred first-line treatment of children and adolescents with T2DM. The recommendations suggest integrating lifestyle modifications (ie, diet and exercise) in concert with medication rather than as an isolated initial treatment approach. Guidelines for frequency of monitoring hemoglobin A1c (HbA1c) and finger-stick blood glucose (BG) concentrations are presented. Decisions were made on the basis of a systematic grading of the quality of evidence and strength of recommendation. The clinical practice guideline underwent peer review before it was approved by the AAP. This clinical practice guideline is not intended to replace clinical judgment or establish a protocol for the care of all children with T2DM, and its recommendations may not provide the only appropriate approach to the management of children with T2DM. Providers should consult experts trained in the care of children and adolescents with T2DM when treatment goals are not met or when therapy with insulin is initiated. The AAP acknowledges that some primary care clinicians may not be confident of their ability to successfully treat T2DM in a child because of the child's age, coexisting conditions, and/or other concerns. At any point at which a clinician feels he or she is not adequately trained or is uncertain about treatment, a referral to a pediatric medical subspecialist should be made. If a diagnosis of T2DM is made by a pediatric medical subspecialist, the primary care clinician should develop a comanagement strategy with the subspecialist to ensure that the child continues to receive appropriate care consistent with a medical home model in which the pediatrician partners with parents to ensure that all health needs are met. *Pediatrics* 2013;131:364–382

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KEY WORDS

diabetes, type 2 diabetes mellitus, childhood, youth, clinical practice guidelines, comanagement, management, treatment

ABBREVIATIONS

AAP—American Academy of Pediatrics

AAFP—American Academy of Family Physicians

BG—blood glucose

FDA—US Food and Drug Administration

HbA1c—hemoglobin A1c

PES—Pediatric Endocrine Society

T1DM—type 1 diabetes mellitus

T2DM—type 2 diabetes mellitus

TODAY—Treatment Options for type 2 Diabetes in Adolescents and Youth

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The recommendations in this report do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate.

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Key action statements are as follows:

1. Clinicians must ensure that insulin therapy is initiated for children and adolescents with T2DM who are ketotic or in diabetic ketoacidosis and in whom the distinction between types 1 and 2 diabetes mellitus is unclear and, in usual cases, should initiate insulin therapy for patients
 - a. who have random venous or plasma BG concentrations ≥ 250 mg/dL; or
 - b. whose HbA1c is $>9\%$.
2. In all other instances, clinicians should initiate a lifestyle modification program, including nutrition and physical activity, and start metformin as first-line therapy for children and adolescents at the time of diagnosis of T2DM.
3. The committee suggests that clinicians monitor HbA1c concentrations every 3 months and intensify treatment if treatment goals for finger-stick BG and HbA1c concentrations are not being met (intensification is defined in the Definitions box).
4. The committee suggests that clinicians advise patients to monitor finger-stick BG (see Key Action Statement 4 in the guideline for further details) concentrations in patients who
 - a. are taking insulin or other medications with a risk of hypoglycemia; or
 - b. are initiating or changing their diabetes treatment regimen; or
 - c. have not met treatment goals; or
 - d. have intercurrent illnesses.
5. The committee suggests that clinicians incorporate the Academy of Nutrition and Dietetics' *Pediatric Weight Management Evidence-Based Nutrition Practice Guidelines* in their dietary or nutrition counseling of patients with T2DM at the time of diagnosis and as part of ongoing management.
6. The committee suggests that clinicians encourage children and adolescents with T2DM to engage in moderate-to-vigorous exercise for at least 60 minutes daily and to limit nonacademic "screen time" to less than 2 hours a day.

Definitions

Adolescent: an individual in various stages of maturity, generally considered to be between 12 and 18 years of age.

Childhood T2DM: disease in the child who typically

- is overweight or obese (BMI $\geq 85^{\text{th}}$ – 94^{th} and $>95^{\text{th}}$ percentile for age and gender, respectively);
- has a strong family history of T2DM;
- has substantial residual insulin secretory capacity at diagnosis (reflected by normal or elevated insulin and C-peptide concentrations);
- has insidious onset of disease;
- demonstrates insulin resistance (including clinical evidence of polycystic ovarian syndrome or acanthosis nigricans);
- lacks evidence for diabetic autoimmunity (negative for autoantibodies typically associated with T1DM). These patients are more likely to have hypertension and dyslipidemia than are those with T1DM.

Clinician: any provider within his or her scope of practice; includes medical practitioners (including physicians and physician extenders), dietitians, psychologists, and nurses.

Diabetes: according to the American Diabetes Association criteria, defined as

1. HbA1c $\geq 6.5\%$ (test performed in an appropriately certified laboratory); or
2. fasting (defined as no caloric intake for at least 8 hours) plasma glucose ≥ 126 mg/dL (7.0 mmol/L); or
3. 2-hour plasma glucose ≥ 200 mg/dL (11.1 mmol/L) during an oral glucose tolerance test performed as described by the World Health Organization by using a glucose load containing the equivalent of 75 g anhydrous glucose dissolved in water; or
4. a random plasma glucose ≥ 200 mg/dL (11.1 mmol/L) with symptoms of hyperglycemia.

(In the absence of unequivocal hyperglycemia, criteria 1–3 should be confirmed by repeat testing.)

Diabetic ketoacidosis: acidosis resulting from an absolute or relative insulin deficiency, causing fat breakdown and formation of β hydroxybutyrate. Symptoms include nausea, vomiting, dehydration, Kussmaul respirations, and altered mental status.

Fasting blood glucose: blood glucose obtained before the first meal of the day and after a fast of at least 8 hours.

Glucose toxicity: The effect of high blood glucose causing both insulin resistance and impaired β -cell production of insulin.

Intensification: Increase frequency of blood glucose monitoring and adjustment of the dose and type of medication in an attempt to normalize blood glucose concentrations.

Intercurrent illnesses: Febrile illnesses or associated symptoms severe enough to cause the patient to stay home from school and/or seek medical care.

Microalbuminuria: Albumin:creatinine ratio ≥ 30 mg/g creatinine but < 300 mg/g creatinine.

Moderate hyperglycemia: blood glucose = 180–250 mg/dL.

Moderate-to-vigorous exercise: exercise that makes the individual breathe hard and perspire and that raises his or her heart rate. An easy way to define exercise intensity for patients is the “talk test”: during moderate physical activity a person can talk, but not sing. During vigorous activity, a person cannot talk without pausing to catch a breath.

Obese: BMI ≥ 95 th percentile for age and gender.

Overweight: BMI between the 85th and 94th percentile for age and gender.

Prediabetes: Fasting plasma glucose ≥ 100 –125 mg/dL or 2-hour glucose concentration during an oral glucose tolerance test ≥ 126 but < 200 mg/dL or an HbA1c of 5.7% to 6.4%.

Severe hyperglycemia: blood glucose > 250 mg/dL.

Thiazolidinediones (TZDs): Oral hypoglycemic agents that exert their effect at least in part by activation of the peroxisome proliferator-activated receptor γ .

Type 1 diabetes mellitus (T1DM): Diabetes secondary to autoimmune destruction of β cells resulting in absolute (complete or near complete) insulin deficiency and requiring insulin injections for management.

Type 2 diabetes mellitus (T2DM): The investigators' designation of the diagnosis was used for the purposes of the literature review. The committee acknowledges the distinction between T1DM and T2DM in this population is not always clear cut, and clinical judgment plays an important role. Typically, this diagnosis is made when hyperglycemia is secondary to insulin resistance accompanied by impaired β -cell function resulting in inadequate insulin production to compensate for the degree of insulin resistance.

Youth: used interchangeably with “adolescent” in this document.

INTRODUCTION

Over the past 3 decades, the prevalence of childhood obesity has increased dramatically in North America,^{1–5} ushering in a variety of health problems, including type 2 diabetes mellitus (T2DM), which previously was not typically seen until much later in life. Currently, in the United States, up to 1 in 3 new cases of diabetes mellitus diagnosed in youth younger than 18 years is T2DM

(depending on the ethnic composition of the patient population),^{6,7} with a disproportionate representation in ethnic minorities^{8,9} and occurring most commonly among youth between 10 and 19 years of age.^{5,10} This trend is not limited to the United States but is occurring internationally¹¹; it is projected that by the year 2030, an estimated 366 million people worldwide will have diabetes mellitus.¹²

The rapid emergence of childhood T2DM poses challenges to many physicians who find themselves generally ill-equipped to treat adult diseases encountered in children. Most diabetes education materials designed for pediatric patients are directed primarily to families of children with type 1 diabetes mellitus (T1DM) and emphasize insulin treatment and glucose monitoring, which may or may not be appropriate for children with

T2DM.^{13,14} The National Diabetes Education Program TIP sheets (which can be ordered or downloaded from www.yourdiabetesinfo.org or ndep.nih.gov) provide guidance on healthy eating, physical activity, and dealing with T2DM in children and adolescents, but few other resources are available that are directly targeted at youth with this disease.¹⁵ Most medications used for T2DM have been tested for safety and efficacy only in people older than 18 years, and there is scant scientific evidence for optimal management of children with T2DM.^{16,17} Recognizing the scarcity of evidence-based data, this report provides a set of guidelines for the management and treatment of children with T2DM that is based on a review of current medical literature covering a period from January 1, 1990, to July 1, 2008.

Despite these limitations, the practicing physician is likely to be faced with the need to provide care for children with T2DM. Thus, the American Academy of Pediatrics (AAP), the Pediatric Endocrine Society (PES), the American Academy of Family Physicians (AAFP), American Diabetes Association, and the Academy of Nutrition and Dietetics (formerly the American Dietetic Association) partnered to develop a set of guidelines that might benefit endocrinologists and generalists, including pediatricians and family physicians alike. This clinical practice guideline may not provide the only appropriate approach to the management of children with T2DM. It is not expected to serve as a sole source of guidance in the management of children and adolescents with T2DM, nor is it intended to replace clinical judgment or establish a protocol for the care of all children with this condition. Rather, it is intended to assist clinicians in decision-making. Primary care providers should endeavor to obtain the requisite skills to care for children and adolescents with

T2DM, and should communicate and work closely with a diabetes team of subspecialists when such consultation is available, practical, and appropriate. The frequency of such consultations will vary, but should usually be obtained at diagnosis and then at least annually if possible. When treatment goals are not met, the committee encourages clinicians to consult with an expert trained in the care of children and adolescents with T2DM.^{18,19} When first-line therapy (eg, metformin) fails, recommendations for intensifying therapy should be generally the same for pediatric and adult populations. The picture is constantly changing, however, as new drugs are introduced, and some drugs that initially appeared to be safe demonstrate adverse effects with wider use. Clinicians should, therefore, remain alert to new developments with regard to treatment of T2DM. Seeking the advice of an expert can help ensure that the treatment goals are appropriately set and that clinicians benefit from cutting-edge treatment information in this rapidly changing area.

The Importance of Family-Centered Diabetes Care

Family structure, support, and education help inform clinical decision-making and negotiations with the patient and family about medical preferences that affect medical decisions, independent of existing clinical recommendations. Because adherence is a major issue in any lifestyle intervention, engaging the family is critical not only to maintain needed changes in lifestyle but also to foster medication adherence.^{20–22} The family's ideal role in lifestyle interventions varies, however, depending on the child's age. Behavioral interventions in younger children have shown a favorable effect. With adolescents, however, interventions based on target-age behaviors (eg, including phone or Internet-based

interventions as well as face-to-face or peer-enhanced activities) appear to foster better results, at least for weight management.²³

Success in making lifestyle changes to attain therapeutic goals requires the initial and ongoing education of the patient and the entire family about healthy nutrition and exercise. Any behavior change recommendations must establish realistic goals and take into account the families' health beliefs and behaviors. Understanding the patient and family's perception of the disease (and overweight status) before establishing a management plan is important to dispel misconceptions and promote adherence.²⁴ Because T2DM disproportionately affects minority populations, there is a need to ensure culturally appropriate, family-centered care along with ongoing education.^{25–28} Several observational studies cite the importance of addressing cultural issues within the family.^{20–22}

Restrictions in Creating This Document

In developing these guidelines, the following restrictions governed the committee's work:

- Although the importance of diabetes detection and screening of at-risk populations is acknowledged and referenced, the guidelines are restricted to patients meeting the diagnostic criteria for diabetes (eg, this document focuses on treatment postdiagnosis). Specifically, this document and its recommendations do not pertain to patients with impaired fasting plasma glucose (100–125 mg/dL) or impaired glucose tolerance (2-hour oral glucose tolerance test plasma glucose: 140–200 mg/dL) or isolated insulin resistance.
- Although it is noted that the distinction between types 1 and 2 diabetes mellitus in children may be

difficult,^{29,30} these recommendations pertain specifically to patients 10 to less than 18 years of age with T2DM (as defined above).

- Although the importance of high-risk care and glycemic control in pregnancy, including pregravid glycemia, is affirmed, the evidence considered and recommendations contained in this document do not pertain to diabetes in pregnancy, including diabetes in pregnant adolescents.
- Recommended screening schedules and management tools for select comorbid conditions (hypertension, dyslipidemia, nephropathy, microalbuminuria, and depression) are provided as resources in the accompanying technical report.³¹ These therapeutic recommendations were adapted from other recommended guideline documents with references, without an independent assessment of their supporting evidence.

METHODS

A systematic review was performed and is described in detail in the accompanying technical report.³¹ To develop the clinical practice guideline on the management of T2DM in children and adolescents, the AAP convened the Subcommittee on Management of T2DM in Children and Adolescents with the support of the American Diabetes Association, the PES, the AAFP, and the Academy of Nutrition and Dietetics. The subcommittee was co-chaired by 2 pediatric endocrinologists preeminent in their field and included experts in general pediatrics, family medicine, nutrition, Native American health, epidemiology, and medical informatics/guideline methodology. All panel members reviewed the AAP policy on Conflict of Interest and Voluntary Disclosure and declared all potential conflicts (see conflicts statements in the Task Force member list).

These groups partnered to develop an evidence report that served as a major source of information for these practice guideline recommendations.³¹ Specific clinical questions addressed in the evidence review were as follows: (1) the effectiveness of treatment modalities for T2DM in children and adolescents, (2) the efficacy of pharmaceutical therapies for treatment of children and adolescents with T2DM, (3) appropriate recommendations for screening for comorbidities typically associated with T2DM in children and adolescents, and (4) treatment recommendations for comorbidities of T2DM in children and adolescents. The accompanying technical report contains more information on comorbidities.³¹

Epidemiologic project staff searched Medline, the Cochrane Collaboration, and Embase. MESH terms used in various combinations in the search included diabetes, mellitus, type 2, type 1, treatment, prevention, diet, pediatric, T2DM, T1DM, NIDDM, metformin, lifestyle, RCT, meta-analysis, child, adolescent, therapeutics, control, adult, obese, gestational, polycystic ovary syndrome, metabolic syndrome, cardiovascular, dyslipidemia, men, and women. In addition, the Boolean

operators NOT, AND, OR were included in various combinations. Articles addressing treatment of diabetes mellitus were prospectively limited to those that were published in English between January 1990 and June 2008, included abstracts, and addressed children between the ages of 120 and 215 months with an established diagnosis of T2DM. Studies in adults were considered for inclusion if >10% of the study population was 45 years of age or younger. The Medline search limits included the following: clinical trial; meta-analysis; randomized controlled trial; review; child: 6–12 years; and adolescent: 13–18 years. Additional articles were identified by review of reference lists of relevant articles and ongoing studies recommended by a technical expert advisory group. All articles were reviewed for compliance with the search limitations and appropriateness for inclusion in this document.

Initially, 199 abstracts were identified for possible inclusion, of which 52 were retained for systematic review. Results of the literature review were presented in evidence tables and published in the final evidence report. An additional literature search of Medline and the Cochrane Database of

| Evidence Quality | Preponderance of Benefit or Harm | Balance of Benefit and Harm |
|--|----------------------------------|-----------------------------|
| A. Well-designed RCTs ^a or diagnostic studies on relevant population | Strong Recommendation | Option |
| B. RCTs or diagnostic studies with minor limitations; overwhelmingly consistent evidence from observational studies | Recommendation | |
| C. Observational studies (case-control and cohort design) | Option | No Rec |
| D. Expert opinion, case reports, reasoning from first principles | Option | No Rec |
| X. Exceptional situations where validating studies cannot be performed and there is a clear preponderance of benefit or harm | Strong Recommendation | |

FIGURE 1

Evidence quality. Integrating evidence quality appraisal with an assessment of the anticipated balance between benefits and harms if a policy is carried out leads to designation of a policy as a strong recommendation, recommendation, option, or no recommendation.³² RCT, randomized controlled trial; Rec, recommendation.

TABLE 1 Definitions and Recommendation Implications

| Statement | Definition | Implication |
|-----------------------|--|---|
| Strong recommendation | A <i>strong recommendation</i> in favor of a particular action is made when the anticipated benefits of the recommended intervention clearly exceed the harms (as a strong recommendation against an action is made when the anticipated harms clearly exceed the benefits) and the quality of the supporting evidence is excellent. In some clearly identified circumstances, strong recommendations may be made when high-quality evidence is impossible to obtain and the anticipated benefits strongly outweigh the harms. | Clinicians should follow a strong recommendation unless a clear and compelling rationale for an alternative approach is present. |
| Recommendation | A <i>recommendation</i> in favor of a particular action is made when the anticipated benefits exceed the harms but the quality of evidence is not as strong. Again, in some clearly identified circumstances, recommendations may be made when high-quality evidence is impossible to obtain but the anticipated benefits outweigh the harms. | Clinicians would be prudent to follow a recommendation but should remain alert to new information and sensitive to patient preferences. |
| Option | <i>Options</i> define courses that may be taken when either the quality of evidence is suspect or carefully performed studies have shown little clear advantage to 1 approach over another. | Clinicians should consider the option in their decision-making, and patient preference may have a substantial role. |
| No recommendation | <i>No recommendation</i> indicates that there is a lack of pertinent published evidence and that the anticipated balance of benefits and harms is presently unclear. | Clinicians should be alert to new published evidence that clarifies the balance of benefit versus harm. |

It should be noted that, because childhood T2DM is a relatively recent medical phenomenon, there is a paucity of evidence for many or most of the recommendations provided. In some cases, supporting references for a specific recommendation are provided that do not deal specifically with childhood T2DM, such as T1DM, childhood obesity, or childhood "prediabetes," or that were not included in the original comprehensive search. Committee members have made every effort to identify those references that did not affect or alter the level of evidence for specific recommendations.

Systematic Reviews was performed in July 2009 for articles discussing recommendations for screening and treatment of 5 recognized comorbidities of T2DM: cardiovascular disease, dyslipidemia, retinopathy, nephropathy, and peripheral vascular disease. Search criteria were the same as for the search on treatment of T2DM, with the inclusion of the term "type 1 diabetes mellitus." Search terms included, in various combinations, the following: diabetes, mellitus, type 2, type 1, pediatric, T2DM, T1DM, NIDDM, hyperlipidemia, retinopathy, microalbuminuria, comorbidities, screening, RCT, meta-analysis, child, and adolescent. Boolean operators and search limits mirrored those of the primary search.

An additional 336 abstracts were identified for possible inclusion, of which 26 were retained for systematic review. Results of this subsequent literature review were also presented in evidence tables and published in

the final evidence report. An epidemiologist appraised the methodologic quality of the research before it was considered by the committee members.

The evidence-based approach to guideline development requires that the evidence in support of each key action statement be identified, appraised, and summarized and that an explicit link between evidence and recommendations be defined. Evidence-based recommendations reflect the quality of evidence and the balance of benefit and harm that is anticipated when the recommendation is followed. The AAP policy statement, "Classifying Recommendations for Clinical Practice Guidelines,"³² was followed in designating levels of recommendation (see Fig 1 and Table 1).

To ensure that these recommendations can be effectively implemented, the Guidelines Review Group at Yale Center for Medical Informatics provided feedback

on a late draft of these recommendations, using the GuideLine Implementability Appraisal.³³ Several potential obstacles to successful implementation were identified and resolved in the final guideline. Evidence was incorporated systematically into 6 key action statements about appropriate management facilitated by BRIDGE-Wiz software (Building Recommendations in a Developer's Guideline Editor; Yale Center for Medical Informatics).

A draft version of this clinical practice guideline underwent extensive peer review by 8 groups within the AAP, the American Diabetes Association, PES, AAFP, and the Academy of Nutrition and Dietetics. Members of the subcommittee were invited to distribute the draft to other representatives and committees within their specialty organizations. The resulting comments were reviewed by the subcommittee and incorporated into the guideline, as appropriate. All AAP guidelines are reviewed every 5 years.

KEY ACTION STATEMENTS

Key Action Statement 1

Clinicians must ensure that insulin therapy is initiated for children and adolescents with T2DM who are ketotic or in diabetic ketoacidosis and in whom the distinction between T1DM and T2DM is unclear; and, in usual cases, should initiate insulin therapy for patients:

- a. who have random venous or plasma BG concentrations ≥ 250 mg/dL; or
- b. whose HbA1c is $>9\%$.

(Strong Recommendation: evidence quality X, validating studies cannot be performed, and C, observational studies and expert opinion; preponderance of benefit over harm.)

Action Statement Profile KAS 1

| | |
|-----------------------------|--|
| Aggregate evidence quality | X (validating studies cannot be performed) |
| Benefits | Avoidance of progression of diabetic ketoacidosis (DKA) and worsening metabolic acidosis; resolution of acidosis and hyperglycemia; avoidance of coma and/or death. Quicker restoration of glycemic control, potentially allowing islet β cells to “rest and recover,” increasing long-term adherence to treatment; avoiding progression to DKA if T1DM. Avoiding hospitalization. Avoidance of potential risks associated with the use of other agents (eg, abdominal discomfort, bloating, loose stools with metformin; possible cardiovascular risks with sulfonylureas). |
| Harms/risks/cost | Potential for hypoglycemia, insulin-induced weight gain, cost, patient discomfort from injection, necessity for BG testing, more time required by the health care team for patient training. |
| Benefits-harms assessment | Preponderance of benefit over harm. |
| Value judgments | Extensive clinical experience of the expert panel was relied on in making this recommendation. |
| Role of patient preferences | Minimal. |
| Exclusions | None. |
| Intentional vagueness | None. |
| Strength | Strong recommendation. |

The presentation of T2DM in children and adolescents varies according to the disease stage. Early in the disease, before diabetes diagnostic criteria are met, insulin resistance predominates with compensatory high insulin secretion, resulting in normoglycemia. Over time, β cells lose their ability to secrete adequate amounts of insulin to overcome insulin resistance, and hyperglycemia results. Early in this

process, blood glucose (BG) concentrations may be normal much of the time and the patient likely will be asymptomatic. At this stage, the disease may only be detected by abnormal BG concentrations identified during screening. As insulin secretion declines further, the patient is likely to develop symptoms of hyperglycemia, occasionally with ketosis or frank ketoacidosis. High glucose concentrations can cause a reversible toxicity to islet β cells that contributes further to insulin deficiency. Of adolescents in whom T2DM is subsequently diagnosed, 5% to 25% present with ketoacidosis.³⁴

Diabetic ketoacidosis must be treated with insulin and fluid and electrolyte replacement to prevent worsening

metabolic acidosis, coma, and death. Children and adolescents with symptoms of hyperglycemia (polyuria, polydipsia, and polyphagia) who are diagnosed with diabetes mellitus should be evaluated for ketosis (serum or urine ketones) and, if positive, for ketoacidosis (venous pH), even if their phenotype and risk factor status (obesity, acanthosis nigricans, positive family history of T2DM) suggests

T2DM. Patients in whom ketoacidosis is diagnosed require immediate treatment with insulin and fluid replacement in an inpatient setting under the supervision of a physician who is experienced in treating this complication.

Youth and adolescents who present with T2DM with poor glycemic control (BG concentrations ≥ 250 mg/dL or HbA1c $>9\%$) but who lack evidence of ketosis or ketoacidosis may also benefit from initial treatment with insulin, at least on a short-term basis.³⁴ This allows for quicker restoration of glycemic control and, theoretically, may allow islet β cells to “rest and recover.”^{35,36} Furthermore, it has been noted that initiation of insulin may increase long-term adherence to treatment in children and adolescents with T2DM by enhancing the patient's perception of the seriousness of the disease.^{7,37–40} Many patients with T2DM can be weaned gradually from insulin therapy and subsequently managed with metformin and lifestyle modification.³⁴

As noted previously, in some children and adolescents with newly diagnosed diabetes mellitus, it may be difficult to distinguish between type 1 and type 2 disease (eg, an obese child presenting with ketosis).^{39,41} These patients are best managed initially with insulin therapy while appropriate tests are performed to differentiate between T1DM and T2DM. The care of children and adolescents who have either newly diagnosed T2DM or undifferentiated-type diabetes and who require initial insulin treatment should be supervised by a physician experienced in treating diabetic patients with insulin.

Key Action Statement 2

In all other instances, clinicians should initiate a lifestyle modification program, including nutrition

and physical activity, and start metformin as first-line therapy for children and adolescents at the time of diagnosis of T2DM. (Strong recommendation: evidence quality B; 1 RCT showing improved outcomes with metformin versus lifestyle; preponderance of benefits over harms.)

Action Statement Profile KAS 2

| | |
|-----------------------------|---|
| Aggregate evidence quality | B (1 randomized controlled trial showing improved outcomes with metformin versus lifestyle combined with expert opinion). |
| Benefit | Lower HbA1c, target HbA1c sustained longer, less early deterioration of BG, less chance of weight gain, improved insulin sensitivity, improved lipid profile. |
| Harm (of using metformin) | Gastrointestinal adverse effects or potential for lactic acidosis and vitamin B ₁₂ deficiency, cost of medications, cost to administer, need for additional instruction about medication, self-monitoring blood glucose (SMBG), perceived difficulty of insulin use, possible metabolic deterioration if T1DM is misdiagnosed and treated as T2DM, potential risk of lactic acidosis in the setting of ketosis or significant dehydration. It should be noted that there have been no cases reported of vitamin B ₁₂ deficiency or lactic acidosis with the use of metformin in children. |
| Benefits-harms assessment | Preponderance of benefit over harm. |
| Value judgments | Committee members valued faster achievement of BG control over not medicating children. |
| Role of patient preferences | Moderate; precise implementation recommendations likely will be dictated by patient preferences regarding healthy nutrition, potential medication adverse reaction, exercise, and physical activity. |
| Exclusions | Although the recommendation to start metformin applies to all, certain children and adolescents with T2DM will not be able to tolerate metformin. In addition, certain older or more debilitated patients with T2DM may be restricted in the amount of moderate-to-vigorous exercise they can perform safely. Nevertheless, this recommendation applies to the vast majority of children and adolescents with T2DM. |
| Intentional vagueness | None. |
| Policy level | Strong recommendation. |

Metformin as First-Line Therapy

Because of the low success rate with diet and exercise alone in pediatric patients diagnosed with T2DM, metformin should be initiated along with the promotion of lifestyle changes, unless insulin is needed to reverse glucose toxicity in the case of significant hyperglycemia or ketoacidosis (see Key Action Statement 1). Because gastrointestinal adverse effects are common with metformin therapy, the

committee recommends starting the drug at a low dose of 500 mg daily, increasing by 500 mg every 1 to 2 weeks, up to an ideal and maximum dose of 2000 mg daily in divided doses.⁴¹ It should be noted that the main gastrointestinal adverse effects (abdominal pain, bloating, loose stools) present at initiation of metformin often are transient and often

disappear completely if medication is continued. Generally, doses higher than 2000 mg daily do not provide additional therapeutic benefit.^{34,42,43} In addition, the use of extended-release metformin, especially with evening dosing, may be considered, although data regarding the frequency of adverse effects with this preparation are scarce. Metformin is generally better tolerated when taken with food. It is important to recognize the paucity of

credible RCTs in adolescents with T2DM. The evidence to recommend initiating metformin at diagnosis along with lifestyle changes comes from 1 RCT, several observational studies, and consensus recommendations.

Lifestyle modifications (including nutrition interventions and increased physical activity) have long been the cornerstone of therapy for T2DM. Yet, medical practitioners recognize that effecting these changes is both challenging and often accompanied by regression over time to behaviors not conducive to maintaining the target range of BG concentrations. In pediatric patients, lifestyle change is most likely to be successful when a multidisciplinary approach is used and the entire family is involved. (Encouragement of healthy eating and physical exercise are discussed in Key Action Statements 5 and 6.) Unfortunately, efforts at lifestyle change often fail for a variety of reasons, including high rates of loss to follow-up; a high rate of depression in teenagers, which affects adherence; and peer pressure to participate in activities that often center on unhealthy eating.

Expert consensus is that fewer than 10% of pediatric T2DM patients will attain their BG goals through lifestyle interventions alone.^{6,35,44} It is possible that the poor long-term success rates observed from lifestyle interventions stem from patients' perception that the intervention is not important because medications are not being prescribed. One might speculate that prescribing medications, particularly insulin therapy, may convey a greater degree of concern for the patient's health and the seriousness of the diagnosis, relative to that conveyed when medications are not needed, and that improved treatment adherence and follow-up may result from the use of medication. Indeed, 2 prospective observational studies revealed that treatment with

lifestyle modification alone is associated with a higher rate of loss to follow-up than that found in patients who receive medication.⁴⁵

Before initiating treatment with metformin, a number of important considerations must be taken into account. First, it is important to determine whether the child with a new diagnosis has T1DM or T2DM, and it is critical to err on the side of caution if there is any uncertainty. The 2009 *Clinical Practice Consensus Guidelines on Type 2 Diabetes in Children and Adolescents* from the International Society for Pediatric and Adolescent Diabetes provides more information on the classification of diabetes in children and adolescents with new diagnoses.⁴⁶ If the diagnosis is unclear (as may be the case when an obese child with diabetes presents also with ketosis), the adolescent must be treated with insulin until the T2DM diagnosis is confirmed.⁴⁷ Although it is recognized that some children with newly diagnosed T2DM may respond to metformin alone, the committee believes that the presence of either ketosis or ketoacidosis dictates an absolute initial requirement for insulin replacement. (This is addressed in Key Action Statement 1.) Although there is little debate that a child presenting with significant hyperglycemia and/or ketosis requires insulin, children presenting with more modest levels of hyperglycemia (eg, random BG of 200–249 mg/dL) or asymptomatic T2DM present additional therapeutic challenges to the clinician. In such cases, metformin alone, insulin alone, or metformin with insulin all represent reasonable options. Additional agents are likely to become reasonable options for initial pharmacologic management in the near future. Although metformin and insulin are the only antidiabetic agents currently approved by the US Food and

Drug Administration (FDA) for use in children, both thiazolidinediones and incretins are occasionally used in adolescents younger than 18 years.⁴⁸

Metformin is recommended as the initial pharmacologic agent in adolescents presenting with mild hyperglycemia and without ketonuria or severe hyperglycemia. In addition to improving hepatic insulin sensitivity, metformin has a number of practical advantages over insulin:

- Potential weight loss or weight neutrality.^{37,48}
- Because of a lower risk of hypoglycemia, less frequent finger-stick BG measurements are required with metformin, compared with insulin therapy or sulfonylureas.^{37,42,49–51}
- Improves insulin sensitivity and may normalize menstrual cycles in females with polycystic ovary syndrome. (Because metformin may also improve fertility in patients with polycystic ovary syndrome, contraception is indicated for sexually active patients who wish to avoid pregnancy.)
- Taking pills does not have the discomfort associated with injections.
- Less instruction time is required to start oral medication, making it is easier for busy practitioners to prescribe.
- Adolescents do not always accept injections, so oral medication might enhance adherence.⁵²

Potential advantages of insulin over metformin for treatment at diabetes onset include the following:

- Metabolic control may be achieved more rapidly with insulin compared with metformin therapy.³⁷
- With appropriate education and targeting the regimen to the individual, adolescents are able to accept and use insulin therapy with improved metabolic outcomes.⁵³

- Insulin offers theoretical benefits of improved metabolic control while preserving β -cell function or even reversing β -cell damage.^{34,35}
- Initial use of insulin therapy may convey to the patient a sense of seriousness of the disease.^{7,53}

Throughout the writing of these guidelines, the authors have been following the progress of the National Institute of Diabetes and Digestive and Kidney Diseases–supported Treatment Options for type 2 Diabetes in Adolescents and Youth (TODAY) trial,⁵⁴ designed to compare standard (metformin alone) therapy versus more aggressive therapy as the initial treatment of youth with recent-onset T2DM. Since the completion of these guidelines, results of the TODAY trial have become available and reveal that metformin alone is inadequate in effecting sustained glycemic control in the majority of youth with diabetes. The study also revealed that the addition of rosiglitazone to metformin is superior to metformin alone in preserving glycemic control. Direct application of these findings to clinical practice is problematic, however, because rosiglitazone is not FDA-approved for use in children, and its use, even in adults, is now severely restricted by the FDA because of serious adverse effects reported in adults. Thus, the results suggest that therapy that is more aggressive than metformin monotherapy may be required in these adolescents to prevent loss of glycemic control, but they do not provide specific guidance because it is not known whether the effect of the additional agent was specific to rosiglitazone or would be seen with the addition of other agents. Unfortunately, there are limited data for the use of other currently available oral or injected hypoglycemic agents in this age range, except for insulin. Therefore,

the writing group for these guidelines continues to recommend metformin as first-line therapy in this age group but with close monitoring for glycemic deterioration and the early addition of insulin or another pharmacologic agent if needed.

Lifestyle Modification, Including Nutrition and Physical Activity

Although lifestyle changes are considered indispensable to reaching treatment goals in diabetes, no significant data from RCTs provide information on success rates with such an approach alone.

A potential downside for initiating lifestyle changes alone at T2DM onset is potential loss of patients to follow-up and worse health outcomes. The value of lifestyle modification in the management of adolescents with T2DM is likely forthcoming after a more detailed analysis of the lifestyle intervention arm of the multicenter TODAY trial becomes available.⁵⁴ As noted previously, although it was published after

plus-rosiglitazone intervention in maintaining glycemic control over time.⁵⁴

Summary

As noted previously, metformin is a safe and effective agent for use at the time of diagnosis in conjunction with lifestyle changes. Although observational studies and expert opinion strongly support lifestyle changes as a key component of the regimen in addition to metformin, randomized trials are needed to delineate whether using lifestyle options alone is a reasonable first step in treating any select subgroups of children with T2DM.

Key Action Statement 3

The committee suggests that clinicians monitor HbA1c concentrations every 3 months and intensify treatment if treatment goals for BG and HbA1c concentrations are not being met. (Option: evidence quality D; expert opinion and studies in children with T1DM and in adults with T2DM; preponderance of benefits over harms.)

evaluated the relationship between glycemic control and the risk of developing microvascular and/or macrovascular complications in children and adolescents with T2DM. A number of studies of children with T1DM^{55–57} and adults with T2DM have, however, shown a significant relationship between glycemic control (as measured by HbA1c concentration) and the risk of microvascular complications (eg, retinopathy, nephropathy, and neuropathy).^{58,59} The relationship between HbA1c concentration and risk of microvascular complications appears to be curvilinear; the lower the HbA1c concentration, the lower the downstream risk of microvascular complications, with the greatest risk reduction seen at the highest HbA1c concentrations.⁵⁷

It is generally recommended that HbA1c concentrations be measured every 3 months.⁶⁰ For adults with T1DM, the American Diabetes Association recommends target HbA1c concentrations of less than 7%; the American Association of Clinical Endocrinologists recommends target concentrations of less than 6.5%. Although HbA1c target concentrations for children and adolescents with T1DM are higher,¹⁵ several review articles suggest target HbA1c concentrations of less than 7% for children and adolescents with T2DM.^{40,61–63} The committee concurs that, ideally, target HbA1c concentration should be less than 7% but notes that specific goals must be achievable for the individual patient and that this concentration may not be applicable for all patients. For patients in whom a target concentration of less than 7% seems unattainable, individualized goals should be set, with the ultimate goal of reaching guideline target concentrations. In addition, in the absence of hypoglycemia, even lower HbA1c target concentrations can be considered on the basis of an absence of hypoglycemic events and other individual considerations.

Action Statement Profile KAS 3

| | |
|-----------------------------|---|
| Aggregate evidence quality | D (expert opinion and studies in children with T1DM and in adults with T2DM; no studies have been performed in children and adolescents with T2DM). |
| Benefit | Diminishing the risk of progression of disease and deterioration resulting in hospitalization; prevention of microvascular complications of T2DM. |
| Harm | Potential for hypoglycemia from overintensifying treatment to reach HbA1c target goals; cost of frequent testing and medical consultation; possible patient discomfort. |
| Benefits-harms assessment | Preponderance of benefits over harms. |
| Value judgments | Recommendation dictated by widely accepted standards of diabetic care. |
| Role of patient preferences | Minimal; recommendation dictated by widely accepted standards of diabetic care. |
| Exclusions | None. |
| Intentional vagueness | Intentional vagueness in the recommendation as far as setting goals and intensifying treatment attributable to limited evidence. |
| Policy level | Option. |

this guideline was developed, the TODAY trial indicated that results from the metformin-plus-lifestyle intervention were not significantly different from either metformin alone or the metformin-

HbA1c provides a measure of glycemic control in patients with diabetes mellitus and allows an estimation of the individual's average BG over the previous 8 to 12 weeks. No RCTs have

When concentrations are found to be above the target, therapy should be intensified whenever possible, with the goal of bringing the concentration to target. Intensification activities may include, but are not limited to, increasing the frequency of clinic visits, engaging in more frequent BG monitoring, adding 1 or more antidiabetic agents, meeting with a registered dietitian and/or diabetes educator, and increasing attention to diet and exercise regimens. Patients whose HbA1c concentrations remain relatively stable may only need to be tested every 6 months. Ideally, real-time HbA1c concentrations should be available at the time of the patient's visit with the clinician to allow the physician and patient and/or parent to discuss intensification of therapy during the visit, if needed.

Key Action Statement 4

The committee suggests that clinicians advise patients to monitor finger-stick BG concentrations in those who

- a. are taking insulin or other medications with a risk of hypoglycemia; or**
- b. are initiating or changing their diabetes treatment regimen; or**
- c. have not met treatment goals; or**
- d. have intercurrent illnesses.**

(Option: evidence quality D; expert consensus. Preponderance of benefits over harms.)

Glycemic control correlates closely with the frequency of BG monitoring in adolescents with T1DM.^{64,65} Although studies evaluating the efficacy of frequent BG monitoring have not been conducted in children and adolescents with T2DM, benefits have been described in insulin-treated adults with T2DM who tested their BG 4 times per day, compared with adults following a less frequent monitoring regimen.⁶⁶ These data support the value of BG monitoring in adults treated with insulin, and likely are relevant to youth with T2DM as well, especially those treated with insulin, at the onset of the disease, when treatment goals are not met, and when the treatment regimen is changed. The committee believes that current (2011) ADA recommendations for finger-stick BG monitoring apply to most youth with T2DM⁶⁷:

- Finger-stick BG monitoring should be performed 3 or more times daily for patients using multiple insulin injections or insulin pump therapy.
- For patients using less-frequent insulin injections, noninsulin therapies, or medical nutrition therapy alone, finger-stick BG monitoring may be useful as a guide to the success of therapy.
- To achieve postprandial glucose targets, postprandial finger-stick BG monitoring may be appropriate.

Recognizing that current practices may not always reflect optimal care, a 2004 survey of practices among members of the PES revealed that 36% of pediatric endocrinologists asked their pediatric patients with T2DM to monitor BG concentrations twice daily; 12% asked patients to do so once daily; 13% asked patients to do so 3 times per day; and 12% asked patients to do so 4 times daily.⁶¹ The questionnaire provided to the pediatric endocrinologists did not ask about the frequency of BG monitoring in relationship to the diabetes regimen, however.

Although normoglycemia may be difficult to achieve in adolescents with T2DM, a fasting BG concentration of 70 to 130 mg/dL is a reasonable target for most. In addition, because postprandial hyperglycemia has been associated with increased risk of cardiovascular events in adults, postprandial BG testing may be valuable in select patients. BG concentrations obtained 2 hours after meals (and paired with pre-meal concentrations) provide an index of glycemic excursion, and may be useful in improving glycemic control, particularly for the patient whose fasting plasma glucose is normal but whose HbA1c is not at target.⁶⁸ Recognizing the limited evidence for benefit of FSBG testing in this population, the committee provides suggested guidance for testing frequency, tailored to the medication regimen, as follows:

BG Testing Frequency for Patients With Newly Diagnosed T2DM: Fasting, Premeal, and Bedtime Testing

The committee suggests that all patients with newly diagnosed T2DM, regardless of prescribed treatment plan, should perform finger-stick BG monitoring before meals (including a morning fasting concentration) and

Action Statement Profile KAS 4

| | |
|-----------------------------|---|
| Aggregate evidence quality | D (expert consensus). |
| Benefit | Potential for improved metabolic control, improved potential for prevention of hypoglycemia, decreased long-term complications. |
| Harm | Patient discomfort, cost of materials. |
| Benefits-harms assessment | Benefit over harm. |
| Value judgments | Despite lack of evidence, there were general committee perceptions that patient safety concerns related to insulin use or clinical status outweighed any risks from monitoring. |
| Role of patient preferences | Moderate to low; recommendation driven primarily by safety concerns. |
| Exclusions | None. |
| Intentional vagueness | Intentional vagueness in the recommendation about specific approaches attributable to lack of evidence and the need to individualize treatment. |
| Policy level | Option. |

at bedtime until reasonable metabolic control is achieved.⁶⁹ Once BG concentrations are at target levels, the frequency of monitoring can be modified depending on the medication used, the regimen's intensity, and the patient's metabolic control. Patients who are prone to marked hyperglycemia or hypoglycemia or who are on a therapeutic regimen associated with increased risk of hypoglycemia will require continued frequent BG testing. Expectations for frequency and timing of BG monitoring should be clearly defined through shared goal-setting between the patient and clinician. The adolescent and family members should be given a written action plan stating the medication regimen, frequency and timing of expected BG monitoring, as well as follow-up instructions.

BG Testing Frequency for Patients on Single Insulin Daily Injections and Oral Agents

Single bedtime long-acting insulin: The simplest insulin regimen consists of a single injection of long-acting insulin at bedtime (basal insulin only). The appropriateness of the insulin dose for patients using this regimen is best defined by the fasting/prebreakfast BG test. For patients on this insulin regimen, the committee suggests daily fasting BG measurements. This regimen is associated with some risk of hypoglycemia (especially overnight or fasting hypoglycemia) and may not provide adequate insulin coverage for mealtime ingestions throughout the day, as reflected by fasting BG concentrations in target, but daytime readings above target. In such cases, treatment with meglitinide (Prandin [Novo Nordisk Pharmaceuticals] or Starlix [Novartis Pharmaceuticals]) or a short-acting insulin before meals (see below) may be beneficial.

Oral agents: Once treatment goals are met, the frequency of monitoring can be decreased; however, the committee recommends some continued BG testing for all youth with T2DM, at a frequency determined within the clinical context (e.g. medication regimen, HbA1c, willingness of the patient, etc.). For example, an infrequent or intermittent monitoring schedule may be adequate when the patient is using exclusively an oral agent associated with a low risk of hypoglycemia and if HbA1c concentrations are in the ideal or non-diabetic range. A more frequent monitoring schedule should be advised during times of illness or if symptoms of hyperglycemia or hypoglycemia develop.

Oral agent plus a single injection of a long-acting insulin: Some youth with T2DM can be managed successfully with a single injection of long-acting insulin in conjunction with an oral agent. Twice a day BG monitoring (fasting plus a second BG concentration – ideally 2-hour post prandial) often is recommended, as long as HbA1c and BG concentrations remain at goal and the patient remains asymptomatic.

BG Testing Frequency for Patients Receiving Multiple Daily Insulin Injections (eg, Basal Bolus Regimens): Premeal and Bedtime Testing

Basal bolus regimens are commonly used in children and youth with T1DM and may be appropriate for some youth with T2DM as well. They are the most labor intensive, providing both basal insulin plus bolus doses of short-acting insulin at meals. Basal insulin is provided through either the use of long-acting, relatively peak-free insulin (by needle) or via an insulin pump. Bolus insulin doses are given at meal-time, using one of the rapid-acting insulin analogs. The bolus dose is calculated by using a correction algorithm for the premeal BG concentration as well as a “carb ratio,” in which 1 unit of

a rapid-acting insulin analog is given for “X” grams of carbohydrates ingested (see box below). When using this method, the patient must be willing and able to count the number of grams of carbohydrates in the meal and divide by the assigned “carb ratio (X)” to know how many units of insulin should be taken. In addition, the patient must always check BG concentrations before the meal to determine how much additional insulin should be given as a correction dose using an algorithm assigned by the care team if the fasting BG is not in target. Insulin pumps are based on this concept of “basal-bolus” insulin administration and have the capability of calculating a suggested bolus dosage, based on inputted grams of carbohydrates and BG concentrations. Because the BG value determines the amount of insulin to be given at each meal, the recommended testing frequency for patients on this regimen is before every meal.

Box 1 Example of Basal Bolus Insulin Regimen

If an adolescent has a BG of 250 mg/dL, is to consume a meal containing 60 g of carbohydrates, with a carbohydrate ratio of 1:10 and an assigned correction dose of 1:25 > 125 (with 25 being the insulin sensitivity and 125 mg/dL the target blood glucose level), the mealtime bolus dose of insulin would be as follows:

60 g/10 “carb ratio” =

6 units rapid-acting insulin for meal

plus

$(250 - 125) / 25 = 125 / 25 =$

5 units rapid-acting insulin for correction

Thus, total bolus insulin coverage at mealtime is: **11 U** (6 + 5) of rapid-acting insulin.

Key Action Statement 5

The committee suggests that clinicians incorporate the Academy of Nutrition and Dietetics' *Pediatric Weight Management Evidence-Based Nutrition Practice Guidelines* in the nutrition counseling of

patients with T2DM both at the time of diagnosis and as part of ongoing management. (Option; evidence quality D; expert opinion; preponderance of benefits over harms. Role of patient preference is dominant.)

agement, summarized below (A complete list of these recommendations is accessible to health care professionals at: <http://www.andevidencelibrary.com/topic.cfm?cat=4102&auth=1>.)

According to the Academy of Nutrition and Dietetics' guidelines, when incorporated with lifestyle changes, balanced macronutrient diets at 900 to 1200 kcal per day are associated with both short- and long-term (eg, ≥ 1 year) improvements in weight status and body composition in children 6 to 12 years of age.⁷⁰ These calorie recommendations are to be incorporated with lifestyle changes, including increased activity and possibly medication. Restrictions of no less than 1200 kcal per day in adolescents 13 to 18 years old result in improved weight status and body composition as well.⁷¹ The Diabetes Prevention Program demonstrated that participants assigned to the intensive lifestyle-intervention arm had a reduction in daily energy intake of 450 kcal and a 58% reduction in progression to diabetes at the 2.8-year follow-up.⁷¹ At the study's end, 50% of the lifestyle-arm participants had achieved the goal weight loss of at least 7% after the 24-week curriculum and 38% showed weight loss of at least 7% at the time of their most recent visit.⁷² The Academy of Nutrition and Dietetics recommends that protein-sparing, modified-fast (ketogenic) diets be restricted to children who are $>120\%$ of their ideal body weight and who have a serious medical complication that would benefit from rapid weight loss.⁷¹ Specific recommendations are for the intervention to be short-term (typically 10 weeks) and to be conducted under the supervision of a multidisciplinary team specializing in pediatric obesity.

Action Statement Profile KAS 5

| | |
|----------------------------|--|
| Aggregate evidence quality | D (expert opinion). |
| Benefit | Promotes weight loss; improves insulin sensitivity; contributes to glycemic control; prevents worsening of disease; facilitates a sense of well-being; and improves cardiovascular health. |
| Harm | Costs of nutrition counseling; inadequate reimbursement of clinicians' time; lost opportunity costs vis-a-vis time and resources spent in other counseling activities. |
| Benefits-harms assessment | Benefit over harm. |
| Value judgments | There is a broad societal agreement on the benefits of dietary recommendations. |
| Role of patient preference | Dominant. Patients may have different preferences for how they wish to receive assistance in managing their weight-loss goals. Some patients may prefer a referral to a nutritionist while others might prefer accessing online sources of help. Patient preference should play a significant role in determining an appropriate weight-loss strategy. |
| Exclusions | None. |
| Intentional vagueness | Intentional vagueness in the recommendation about specific approaches attributable to lack of evidence and the need to individualize treatment. |
| Policy level | Option. |

Consuming more calories than one uses results in weight gain and is a major contributor to the increasing incidence of T2DM in children and adolescents. Current literature is inconclusive about a single best meal plan for patients with diabetes mellitus, however, and studies specifically addressing the diet of children and adolescents with T2DM are limited. Challenges to making recommendations stem from the small sample size of these studies, limited specificity for children and adolescents, and difficulties in generalizing the data from dietary research studies to the general population.

Although evidence is lacking in children with T2DM, numerous studies have been conducted in overweight

children and adolescents, because the great majority of children with T2DM are obese or overweight at diagnosis.²⁶ The committee suggests that clinicians encourage children and adolescents with T2DM to follow the Academy of Nutrition and Dietetics' recommendations for maintaining healthy weight to promote health and reduce obesity in this population. The committee recommends that clinicians refer patients to a registered dietitian who has expertise in the nutritional needs of youth with T2DM. Clinicians should incorporate the Academy of Nutrition and Dietetics' *Pediatric Weight Management Evidence-Based Nutrition Practice Guidelines*, which describe effective, evidence-based treatment options for weight man-

Regardless of the meal plan prescribed, some degree of nutrition education must be provided to maximize adherence and positive results. This education should encourage patients to follow healthy eating patterns, such as consuming 3 meals with planned snacks per day, not eating while watching television or using computers, using smaller plates to make portions appear larger, and leaving small amounts of food on the plate.⁷³ Common dietary recommendations to reduce calorie intake and to promote weight loss in children include the following: (1) eating regular meals and snacks; (2) reducing portion sizes; (3) choosing calorie-free beverages, except for milk; (4) limiting juice to 1 cup per day; (5) increasing consumption of fruits and vegetables; (6) consuming 3 or 4 servings of low-fat dairy products per day; (7) limiting intake of high-fat foods; (8) limiting frequency and size of snacks; and (9) reducing calories consumed in fast-food meals.⁷⁴

Key Action Statement 6

The committee suggests that clinicians encourage children and adolescents with T2DM to engage in moderate-to-vigorous exercise for at least 60 minutes daily and to limit nonacademic screen time to

less than 2 hours per day. (Option: evidence quality D, expert opinion and evidence from studies of metabolic syndrome and obesity; preponderance of benefits over harms. Role of patient preference is dominant.)

Action Statement Profile KAS 6

| | |
|----------------------------|---|
| Aggregate evidence quality | D (expert opinion and evidence from studies of metabolic syndrome and obesity). |
| Benefit | Promotes weight loss; contributes to glycemic control; prevents worsening of disease; facilitates the ability to perform exercise; improves the person's sense of well-being; and fosters cardiovascular health. |
| Harm | Cost for patient of counseling, food, and time; costs for clinician in taking away time that could be spent on other activities; inadequate reimbursement for clinician's time. |
| Benefits-harms assessment | Preponderance of benefit over harm. |
| Value judgments | Broad consensus. |
| Role of patient preference | Dominant. Patients may seek various forms of exercise. Patient preference should play a significant role in creating an exercise plan. |
| Exclusions | Although certain older or more debilitated patients with T2DM may be restricted in the amount of moderate-to-vigorous exercise they can perform safely, this recommendation applies to the vast majority of children and adolescents with T2DM. |
| Intentional vagueness | Intentional vagueness on the sequence of follow-up contact attributable to the lack of evidence and the need to individualize care. |
| Policy level | Option. |

Recommendations From the Academy of Nutrition and Dietetics

Pediatric Weight Management Evidence-Based Nutrition Practice Guidelines

| Recommendation | Strength |
|--|----------|
| Interventions to reduce pediatric obesity should be multicomponent and include diet, physical activity, nutritional counseling, and parent or caregiver participation. | Strong |
| A nutrition prescription should be formulated as part of the dietary intervention in a multicomponent pediatric weight management program. | Strong |
| Dietary factors that may be associated with an increased risk of overweight are increased total dietary fat intake and increased intake of calorically sweetened beverages. | Strong |
| Dietary factors that may be associated with a decreased risk of overweight are increased fruit and vegetable intake. | Strong |
| A balanced macronutrient diet that contains no fewer than 900 kcal per day is recommended to improve weight status in children aged 6–12 y who are medically monitored. | Strong |
| A balanced macronutrient diet that contains no fewer than 1200 kcal per day is recommended to improve weight status in adolescents aged 13–18 y who are medically monitored. | Strong |
| Family diet behaviors that are associated with an increased risk of pediatric obesity are parental restriction of highly palatable foods, consumption of food away from home, increased meal portion size, and skipping breakfast. | Fair |

Engaging in Physical Activity

Physical activity is an integral part of weight management for prevention and treatment of T2DM. Although there is a paucity of available data from children and adolescents with T2DM, several well-controlled studies performed in obese children and adolescents at risk of metabolic syndrome and T2DM provide guidelines for physical activity. (See the Resources section for tools on this subject.) A summary of the references supporting the evidence for this guideline can be found in the technical report.³¹

At present, moderate-to-vigorous exercise of at least 60 minutes daily is recommended for reduction of BMI and improved glycemic control in patients with T2DM.⁷⁵ “Moderate to

vigorous exercise” is defined as exercise that makes the individual breathe hard and perspire and that raises his or her heart rate. An easy way to define exercise intensity for patients is the “talk test”; during moderate physical activity a person can talk but not sing. During vigorous activity, a person cannot talk without pausing to catch a breath.⁷⁶

Adherence may be improved if clinicians provide the patient with a written prescription to engage in physical activity, including a “dose” describing ideal duration, intensity, and frequency.⁷⁵ When prescribing physical exercise, clinicians are encouraged to be sensitive to the needs of children, adolescents, and their families. Routine, organized exercise may be beyond the family’s logistical and/or financial means, and some families may not be able to provide structured exercise programs for their children. It is most helpful to recommend an individualized approach that can be incorporated into the daily routine, is tailored to the patients’ physical abilities and preferences, and recognizes the families’ circumstances.⁷⁷ For example, clinicians might recommend only daily walking, which has been shown to improve weight loss and insulin sensitivity in adults with T2DM⁷⁸ and may constitute “moderate to vigorous activity” for some children with T2DM. It is also important to recognize that the recommended 60 minutes of exercise do not have to be accomplished in 1 session but can be completed through several, shorter increments (eg, 10–15 minutes). Patients should be encouraged to identify a variety of forms of activity that can be performed both easily and frequently.⁷⁷ In addition, providers should be cognizant of the potential need to adjust the medication dosage, especially if the patient is receiving insulin, when initiating an aggressive physical activity program.

Reducing Screen Time

Screen time contributes to a sedentary lifestyle, especially when the child or adolescent eats while watching television or playing computer games. The US Department of Health and Human Services recommends that individuals limit “screen time” spent watching television and/or using computers and handheld devices to less than 2 hours per day unless the use is related to work or homework.⁷⁹ Physical activity may be gained either through structured games and sports or through everyday activities, such as walking, ideally with involvement of the parents as good role models.

Increased screen time and food intake and reduced physical activity are associated with obesity. There is good evidence that modifying these factors can help prevent T2DM by reducing the individual’s rate of weight gain. The evidence profile in pediatric patients with T2DM is inadequate at this time, however. Pending new data, the committee suggests that clinicians follow the AAP Committee on Nutrition’s guideline, *Prevention of Pediatric Overweight and Obesity*. The guideline recommends restricting nonacademic screen time to a maximum of 2 hours per day and discouraging the presence of video screens and television sets in children’s bedrooms.^{80–82} The American Medical Association’s Expert Panel on Childhood Obesity has endorsed this guideline.

Valuable recommendations for enhancing patient health include the following:

- With patients and their families, jointly determining an individualized plan that includes specific goals to reduce sedentary behaviors and increase physical activity.
- Providing a written prescription for engaging in 60-plus minutes of moderate-to-vigorous physical activities per day that includes

dose, timing, and duration. It is important for clinicians to be sensitive to the needs of children, adolescents, and their families in encouraging daily physical exercise. Graded duration of exercise is recommended for those youth who cannot initially be active for 60 minutes daily, and the exercise may be accomplished through several, shorter increments (eg, 10–15 minutes).

- Incorporating physical activities into children’s and adolescents’ daily routines. Physical activity may be gained either through structured games and sports or through everyday activities, such as walking.
- Restricting nonacademic screen time to a maximum of 2 hours per day.
- Discouraging the presence of video screens and television sets in children’s bedrooms.

Conversations pertaining to the Key Action Statements should be clearly documented in the patient’s medical record.

AREAS FOR FUTURE RESEARCH

As noted previously, evidence for medical interventions in children in general is scant and is especially lacking for interventions directed toward children who have developed diseases not previously seen commonly in youth, such as childhood T2DM. Recent studies such as the Search for Diabetes in Youth Study (SEARCH)—an observational multicenter study in 2096 youth with T2DM funded by the Centers for Disease Control and Prevention and the National Institute of Diabetes and Digestive and Kidney Diseases—now provide a detailed description of childhood diabetes. Subsequent trials will describe the short-term and enduring effects of specific interventions

on the progression of the disease with time.

Although it is likely that children and adolescents with T2DM have an aggressive form of diabetes, as reflected by the age of onset, future research should determine whether the associated comorbidities and complications of diabetes also are more aggressive in pediatric populations than in adults and if they are more or less responsive to therapeutic interventions. Additional research should explore whether early introduction of insulin or the use of particular oral agents will preserve β -cell function in these children, and whether recent technologic advances (such as continuous glucose monitoring and insulin pumps) will benefit this population. Additional issues that require further study include the following:

- To delineate whether using lifestyle options without medication is a reliable first step in treating selected children with T2DM.
- To determine whether BG monitoring should be recommended to all children and youth with T2DM, regardless of therapy used; what the optimal frequency of BG monitoring is for pediatric patients on the basis of treatment regimen; and which subgroups will be able to successfully maintain glycemic goals with less frequent monitoring.
- To explore the efficacy of school- and clinic-based diet and physical activity interventions to prevent and manage pediatric T2DM.
- To explore the association between increased "screen time" and reduced physical activity with respect to T2DM's risk factors.

RESOURCES

Several tools are available online to assist providers in improving patient

adherence to lifestyle modifications, including examples of activities to be recommended for patients:

- The American Academy of Pediatrics:
 - www.healthychildren.org
 - www.letsmove.gov
 - Technical Report: Management of Type 2 Diabetes Mellitus in Children and Adolescents.³¹
 - Includes an overview and screening tools for a variety of comorbidities.
 - Gahagan S, Silverstein J; Committee on Native American Child Health and Section on Endocrinology. Clinical report: prevention and treatment of type 2 diabetes mellitus in children, with special emphasis on American Indian and Alaska Native Children. *Pediatrics*. 2003;112(4):e328–e347. Available at: <http://www.pediatrics.org/cgi/content/full/112/4/e328>⁶³
 - Fig 3 presents a screening tool for microalbumin.
 - Bright Futures: <http://brightfutures.aap.org/>
 - Daniels SR, Greer FR; Committee on Nutrition. Lipid screening and cardiovascular health in childhood. *Pediatrics*. 2008;122(1):198–208. Available at: <http://care.diabetesjournals.org/content/26/7/2194.full>
- The American Diabetes Association: www.diabetes.org
 - Management of dyslipidemia in children and adolescents with diabetes. *Diabetes Care*. 2003;26(7):2194–2197. Available at: <http://care.diabetesjournals.org/content/26/7/2194.full>
- Academy of Nutrition and Dietetics:
 - <http://www.eatright.org/childhoodobesity/>
 - <http://www.eatright.org/kids/>
 - <http://www.eatright.org/cps/rde/xchg/ada/hs.xsl/index.html>
- Pediatric Weight Management Evidence-Based Nutrition Practice Guidelines: <http://www.adaevidencelibrary.com/topic.cfm?cat=2721>
- American Heart Association:
 - American Heart Association *Circulation*. 2006 Dec 12;114(24):2710–2738. Epub 2006 Nov 27. Review.
- Centers for Disease Control and Prevention:
 - <http://www.cdc.gov/obesity/childhood/solutions.html>
 - BMI and other growth charts can be downloaded and printed from the CDC Web site: <http://www.cdc.gov/growth-charts>.
 - Center for Epidemiologic Studies Depression Scale (CES-D): <http://www.chcr.brown.edu/pcoc/cesdscale.pdf>; see attachments
- *Diagnostic and Statistical Manual of Mental Disorders*. 4th ed. Washington, DC: American Psychiatric Association; 1994
- Let's Move Campaign: www.letsmove.gov
- The Reach Institute. *Guidelines for Adolescent Depression in Primary Care (GLAD-PC) Toolkit*, 2007. Contains a listing of the criteria for major depressive disorder as defined by the DSM-IV-TR. Available at: <http://www.gladpc.org>
- The National Heart, Lung, and Blood Institute (NHLBI) hypertension guidelines: http://www.nhlbi.nih.gov/guidelines/hypertension/child_tbl.htm
- The National Diabetes Education Program and TIP sheets (including tip sheets on youth transitioning to adulthood and adult providers, Staying Active, Eating Healthy, Ups and Downs of Diabetes, etc): www.ndep.nih.gov or www.yourdiabetesinfo.org

- National High Blood Pressure Education Program Working Group on High Blood Pressure in Children and Adolescents, The Fourth Report on the Diagnosis, Evaluation, and Treatment of High Blood Pressure in Children and Adolescents: *Pediatrics*. 2004;114:555–576. Available at: http://pediatrics.aappublications.org/content/114/Supplement_2/555.long
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- The National Institute of Child Health and Human Development (NICHD): www.NICHD.org
- President's Council on Physical Fitness and Sports: http://www.presidentschallenge.org/home_kids.aspx
- US Department of Agriculture's "My Pyramid" Web site:

- <http://www.choosemyplate.gov/>
- <http://fnic.nal.usda.gov/life-cycle-nutrition/child-nutrition-and-health>

SUBCOMMITTEE ON TYPE 2 DIABETES (OVERSIGHT BY THE STEERING COMMITTEE ON QUALITY IMPROVEMENT AND MANAGEMENT, 2008–2012)

Kenneth Claud Copeland, MD, FAAP: Co-chair—Endocrinology and Pediatric Endocrine Society Liaison (2009: Novo Nordisk, Genentech, Endo [National Advisory Groups]; 2010: Novo Nordisk [National Advisory Group]); published research related to type 2 diabetes

Janet Silverstein, MD, FAAP: Co-chair—Endocrinology and American Diabetes Association Liaison (small grants with Pfizer, Novo Nordisk, and Lilly; grant review committee for Genentech; was on an advisory committee for Sanofi Aventis, and Abbott Laboratories for a 1-time meeting); published research related to type 2 diabetes

Kelly Roberta Moore, MD, FAAP: General Pediatrics, Indian Health, AAP Committee on Native American Child Health Liaison (board member of the Merck Company Foundation

Alliance to Reduce Disparities in Diabetes. Their national program office is the University of Michigan's Center for Managing Chronic Disease.)

Greg Edward Prazar, MD, FAAP: General Pediatrics (no conflicts)

Terry Raymer, MD, CDE: Family Medicine, Indian Health Service (no conflicts)

Richard N. Shiffman, MD, FAAP: Partnership for Policy Implementation Informatician, General Pediatrics (no conflicts)

Shelley C. Springer, MD, MBA, FAAP: Epidemiologist (no conflicts)

Meaghan Anderson, MS, RD, LD, CDE: Academy of Nutrition and Dietetics Liaison (formerly a Certified Pump Trainer for Animas)

Stephen J. Spann, MD, MBA, FAAP: American Academy of Family Physicians Liaison (no conflicts)

Vidhu V. Thaker, MD, FAAP: Qullin Liaison, General Pediatrics (no conflicts)

CONSULTANT

Susan K. Flinn, MA: Medical Writer (no conflicts)

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