CHILDREN AND ADOLESCENTS



# 14. Children and Adolescents: Standards of Medical Care in Diabetes—2022

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American Diabetes Association
Professional Practice Committee\*

The American Diabetes Association (ADA) "Standards of Medical Care in Diabetes" includes the ADA's current clinical practice recommendations and is intended to provide the components of diabetes care, general treatment goals and guidelines, and tools to evaluate quality of care. Members of the ADA Professional Practice Committee, a multidisciplinary expert committee (https://doi.org/10.2337/dc22-SPPC), are responsible for updating the Standards of Care annually, or more frequently as warranted. For a detailed description of ADA standards, statements, and reports, as well as the evidence-grading system for ADA's clinical practice recommendations, please refer to the Standards of Care Introduction (https://doi.org/10.2337/dc22-SINT). Readers who wish to comment on the Standards of Care are invited to do so at professional.diabetes .org/SOC.

The management of diabetes in children and adolescents cannot simply be derived from care routinely provided to adults with diabetes. The epidemiology, pathophysiology, developmental considerations, and response to therapy in pediatric diabetes are often different from adult diabetes. There are also differences in recommended care for children and adolescents with type 1 diabetes, type 2 diabetes, and other forms of pediatric diabetes. This section is divided into two major parts: the first part addresses care for children and adolescents with type 1 diabetes, and the second part addresses care for children and adolescents with type 2 diabetes. Monogenic diabetes (neonatal diabetes and maturity-onset diabetes in the young [MODY]) and cystic fibrosis-related diabetes, which are often present in youth, are discussed in Section 2, "Classification and Diagnosis of Diabetes" (https://doi.org/ 10.2337/dc22-S002). Table 14.1A and Table 14.1B provide an overview of the recommendations for screening and treatment of complications and related conditions in pediatric type 1 diabetes and type 2 diabetes, respectively. In addition to comprehensive diabetes care, youth with diabetes should receive age- and developmentally appropriate pediatric care, including vaccines and immunizations as recommended by the Centers for Disease Control and Prevention (CDC) (1). To ensure continuity of care as an adolescent with diabetes becomes an adult, guidance is provided at the end of this section on the transition from pediatric to adult diabetes care.

Due to the nature of pediatric clinical research, the recommendations for children and adolescents with diabetes are less likely to be based on clinical trial evidence. However, expert opinion and a review of available and relevant experimental data are summarized in the American Diabetes Association (ADA) position statements "Type 1 Diabetes in Children and Adolescents" (2) and "Evaluation and Management of Youth-Onset Type 2 Diabetes" (3). Finally, other sections in the Standards of Care may have recommendations that apply to youth with diabetes and are referenced in the narrative of this section.

\*A complete list of members of the American Diabetes Association Professional Practice Committee can be found at https://doi.org/10.2337/dc22-SPPC.

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|                               | Thyroid disease   | Celiac disease  | Hypertension  | Dyslipidemia   | Nephropathy   | Retinopathy   | Neuropathy  |
|-------------------------------|---|---|---|--|---|---|---|
| Corresponding recommendations | 14.29 and 14.30   | 14.31–14.33   | 14.34–14.37   | 14.38–14.42  | 14.45 and 14.46   | 14.47–14.49   | 14.50   |
| Method                        | Thyroid-stimulating<br>hormone; consider<br>antithyroglobulin and<br>antithyroid<br>peroxidase antibodies                       | lgA tTG if total lgA<br>normal; lgG tTG and<br>deamidated gliadin<br>antibodies if lgA<br>deficient | Blood pressure<br>monitoring  | Lipid profile, nonfasting acceptable initially   | Albumin-to-creatinine ratio; random sample acceptable initially   | Dilated fundoscopy or<br>retinal photography  | Foot exam with foot<br>pulses, pinprick, 10-g<br>monofilament<br>sensation tests,<br>vibration, and ankle<br>reflexes |
| When to start                 | Soon after diagnosis  | Soon after diagnosis  | At diagnosis  | Soon after diagnosis;<br>preferably after<br>glycemia has<br>improved and ≥2<br>years old  | Puberty or >10 years old, whichever is earlier, and diabetes duration of 5 years  | Puberty or ≥11 years old, whichever is earlier, and diabetes duration of 3–5 years                                    | Puberty or ≥10 years old, whichever is earlier, and diabetes duration of 5 years                                      |
| frequency                     | Every 1–2 years if<br>thyroid antibodies<br>negative; more often<br>if symptoms develop<br>or presence of<br>thyroid antibodies | Within 2 years and then at 5 years after diagnosis; sooner if symptoms develop                      | Every visit   | If LDL <pre></pre>   | If normal, annually; if<br>abnormal, repeat<br>with confirmation in<br>two of three samples<br>over 6 months                                | If normal, every 2 years;<br>consider less frequently<br>(every 4 years) if A1C<br><8% and eye<br>professional agrees | If normal, annually   |
| Target                        | NA<br>A   | NA  | <pre>&lt;90th percentile for     age, sex, and height; if ≥13 years old, &lt;120/80 mmHg</pre>  | LDL <100 mg/dL   | Albumin-to-creatinine<br>ratio <30 mg/g   | No retinopathy  | No neuropathy   |
| Treatment                     | Appropriate treatment of underlying thyroid disorder  | After confirmation, start gluten-free diet  | Lifestyle modification for elevated blood pressure (90th to <95th percentile for age, sex, and height or, if ≥13 years old, 120–129/<80 mmHg); lifestyle modification and ACE inhibitor or ARB* for hypertension (≥95th percentile for age, sex, and height or, if ≥13 years old, ≥130/80 mmHg) | If abnormal, optimize glucose control and medical nutrition therapy; if after 6 months LDL > 160 mg/dL or > 130 mg/dL with cardiovascular risk factor(s), initiate statin therapy (for those aged > 10 years)* | Optimize glucose and blood pressure control; ACE inhibitor* if albuminto-creatinine ratio is elevated in two of three samples over 6 months | Optimize glucose control; treatment per ophthalmology   | Optimize glucose control; referral to neurology   |

|                                | Hypertension  | Nephropathy   | Neuropathy   | Retinopathy   | Nonalcoholic<br>fatty liver disease   | Obstructive sleep<br>apnea  | Polycystic ovarian syndrome (for adolescent females)                                      | Dyslipidemia   |
|--------------------------------|---|---|--|---|---|---|---|--|
| Corresponding recom-mendations | 14.77–14.80   | 14.81–14.86   | 14.87 and 14.88  | 14.89–14.92   | 14.93 and 14.94   | 14.95   | 14.96–14.98   | 14.100–14.104  |
| Method                         | Blood pressure<br>monitoring  | Albumin-to-creatinine ratio; random sample acceptable initially   | Foot exam with foot pulses, pinprick, 10-g monofilament sensation tests, vibration, and ankle reflexes | Dilated fundoscopy                                    | AST and ALT<br>measurement  | Screening for symptoms  | Screening for symptoms; laboratory evaluation if positive symptoms                        | Lipid profile  |
| When to start                  | At diagnosis  | At diagnosis  | At diagnosis   | At/soon after<br>diagnosis                            | At diagnosis  | At diagnosis  | At diagnosis  | Soon after diagnosis,<br>preferably after<br>glycemia has<br>improved  |
| Follow-up<br>frequency         | Every visit   | If normal, annually, if<br>abnormal, repeat<br>with confirmation<br>in two of three<br>samples over 6<br>months                             | If normal, annually  | If normal, annually                                   | Annually  | Every visit   | Every visit   | Annually   |
| Target                         | <90th percentile for<br>age, sex, and height;<br>if ≥13 years old,<br><130/80 mmHg  | <30 mg/g  | No neuropathy  | No retinopathy  | N A   | NA  | NA  | LDL <100 mg/dL, HDL >35 mg/dL, triglycerides <150 mg/dL  |
| Treatment                      | Lifestyle modification for elevated blood pressure (90th to <95th percentile for age, sex, and height ov, if ≥13 years old, 120–129/<80 mmHg); lifestyle modification and ACE inhibitor or ARB* for hypertension (≥95th percentile for age, sex, and height or, if ≥13 years, ≥130/80 mmHg) | Optimize glucose and blood pressure control; ACE inhibitor* if albumin to-creatinine ratio is elevated in two of three samples over (months | Optimize glucose control; referral to neurology  | Optimize glucose control; treatment per ophthalmology | Refer to gastro-<br>enterology for<br>persistently<br>elevated or<br>worsening<br>transaminases | If positive symptoms, refer to sleep specialist and polysomnogram | If no contra- indications, oral contraceptive pills; medical nutrition therapy; metformin | If abnormal, optimize glucose control and medical nutrition therapy; if after 6 months, LDL > 130 mg/dL, initiate statin therapy (for those aged > 10 years)*; if triglycerides > 400 mg/dL fasting or > 1,000 mg/dL nonfasting, begin fibrate |
|                                |   |   |  |   |   |   |   |  |

ARB, angiotensin receptor blocker; NA, not applicable. \*Due to the potential teratogenic effects, females should receive reproductive counseling and medication should be avoided in females of childbearing age who are not using reliable contraception.

# **TYPE 1 DIABETES**

Type 1 diabetes is the most common form of diabetes in youth (4), although data suggest that it may account for a large proportion of cases diagnosed in adult life (5). The provider must consider the unique aspects of care and management of children and adolescents with type 1 diabetes, such as changes in insulin sensitivity related to physical growth and sexual maturation, ability to provide self-care, supervision in the childcare and school environment, neurological vulnerability to hypoglycemia and hyperglycemia in young children, and possible adverse neurocognitive effects of diabetic ketoacidosis (DKA) (6,7). Attention to family dynamics, developmental stages, and physiologic differences related to sexual maturity is essential in developing and implementing an optimal diabetes treatment plan (8).

A multidisciplinary team trained in pediatric diabetes management and sensitive to the challenges of children and adolescents with type 1 diabetes and their families should provide diabetesspecific care for this population. It is essential that diabetes self-management education and support, medical nutrition therapy, and psychosocial support be provided at diagnosis and regularly thereafter in a developmentally appropriate format that builds on prior knowledge by a team of health care professionals experienced with the biological, educational, nutritional, behavioral, and emotional needs of the growing child and family. The diabetes team, taking into consideration the youth's developmental and psychosocial needs, should ask about and advise the youth and parents/ caregivers about diabetes management responsibilities on an ongoing basis.

# Diabetes Self-Management Education and Support

## Recommendation

14.1 Youth with type 1 diabetes and their parents/caregivers (for patients aged <18 years) should receive culturally sensitive and developmentally appropriate individualized diabetes self-management education and support according to national standards at diagnosis and routinely thereafter. B

Self-management in pediatric diabetes involves both the youth and their parents/adult caregivers. No matter how sound the medical regimen is, it can only be effective if the family and/ or affected individuals are able to implement it. Family involvement is a vital component of optimal diabetes management throughout childhood and adolescence. As parents/caregivers are critical to diabetes self-management in youth, diabetes care requires an approach that places the youth and their parents/caregivers at the center of the care model. The pediatric diabetes care team must be capable of evaluating the educational, behavioral, emotional, and psychosocial factors that impact the implementation of a treatment plan and must work with the youth and family to overcome barriers or redefine goals as appropriate. Diabetes self-management education and support requires periodic reassessment, especially as the youth grows, develops, and acquires the need and desire for greater independent self-care skills. The pediatric diabetes team should work with the youth and their parents/caregivers to ensure there is not a premature transfer of responsibilities for self-management to the youth during this time. In addition, it is necessary to assess the educational needs and skills of, and provide training to, day care workers, school nurses, and school personnel who are responsible for the care and supervision of the child with diabetes (9–11).

# **Nutrition Therapy**

#### Recommendations

- 14.2 Individualized medical nutrition therapy is recommended for children and adolescents with type 1 diabetes as an essential component of the overall treatment plan. A
- 14.3 Monitoring carbohydrate intake, whether by carbohydrate counting or experience-based estimation, is a key component to optimizing glycemic management. B
- 14.4 Comprehensive nutrition education at diagnosis, with annual updates, by an experienced registered dietitian nutritionist, is recommended to assess

caloric and nutrition intake in relation to weight status and cardiovascular disease risk factors and to inform macronutrient choices. E

Dietary management should be individualized: family habits, food preferences, religious or cultural needs, finances, schedules, physical activity, and the patient's and family's abilities in numeracy, literacy, and self-management should be considered. Visits with a registered dietitian nutritionist should include assessment for changes in food preferences over time, access to food, growth and development, weight status, cardiovascular risk, and potential for disordered eating. Dietary adherence is associated with better glycemic control in youth with type 1 diabetes (12).

#### Physical Activity and Exercise

- 14.5 Physical activity is recommended for all youth with type 1 diabetes with the goal of 60 min of moderate- to vigorous-intensity aerobic activity daily, with vigorous muscle-strengthening and bone-strengthening activities at least 3 days per week. C
- 14.6 Frequent glucose monitoring before, during, and after exercise, via blood glucose meter or continuous glucose monitoring, is important to prevent, detect, and treat hypoglycemia and hyperglycemia associated with exercise. C
- 14.7 Youth and their parents/caregivers should receive education on targets and management of glycemia before, during, and after physical activity, individualized according to the type and intensity of the planned physical activity. E
- 14.8 Youth and their parents/caregivers should be educated on
  strategies to prevent hypoglycemia during, after, and overnight following physical activity
  and exercise, which may
  include reducing prandial insulin dosing for the meal/snack
  preceding (and, if needed,
  following) exercise, reducing

basal insulin doses, increasing carbohydrate intake, eating bedtime snacks, and/or using continuous glucose monitoring. Treatment for hypoglycemia should be accessible before, during, and after engaging in activity. C

Physical activity and exercise positively impact metabolic and psychological health in children with type 1 diabetes (13). While it affects insulin sensitivity, physical fitness, strength building, weight management, social interaction, mood, selfesteem building, and the creation of healthful habits for adulthood, it also has the potential to cause both hypoglycemia and hyperglycemia.

See below for strategies to mitigate hypoglycemia risk and minimize hyperglycemia associated with exercise. For an in-depth discussion, see recently published reviews and guidelines (14-16).

Overall, it is recommended that youth participate in 60 min of moderate- (e.g., brisk walking, dancing) to vigorous- (e.g., running, jumping rope) intensity aerobic activity daily, including resistance and flexibility training (17). Although uncommon in the pediatric population, patients should be medically evaluated for comorbid conditions or diabetes complications that may restrict participation in an exercise program. As hyperglycemia can occur before, during, and after physical activity, it is important to ensure that the elevated glucose level is not related to insulin deficiency that would lead to worsening hyperglycemia with exercise and ketosis risk. Intense activity should be postponed with marked hyperglycemia (glucose ≥350 mg/dL [19.4 mmol/ L]), moderate to large urine ketones, and/or  $\beta$ -hydroxybutyrate (B-OHB) >1.5 mmol/L. Caution may be needed when B-OHB levels are  $\geq$ 0.6 mmol/L (12,14).

The prevention and treatment of hypoglycemia associated with physical activity include decreasing the prandial insulin for the meal/snack before exercise and/or increasing food intake. Patients on insulin pumps can lower basal rates by  $\sim$ 10–50% or more or suspend for 1-2 h during exercise (18). Decreasing basal rates or long-acting insulin doses by  ${\sim}20\%$  after exercise

may reduce delayed exercise-induced hypoglycemia (19). Accessible rapid-acting carbohydrates and frequent blood glucose monitoring before, during, and after exercise, with or without continuous glucose monitoring (CGM), maximize safety with exercise.

Blood glucose targets prior to physical activity and exercise should be 126-180 mg/dL (7.0-10.0 mmol/L) but should be individualized based on the type, intensity, and duration of activity (14,20). Consider additional carbohydrate intake during and/or after exercise, depending on the duration and intensity of physical activity, to prevent hypoglycemia. For low- to moderate-intensity aerobic activities (30-60 min), and if the youth is fasting, 10-15 g of carbohydrate may prevent hypoglycemia (21). After insulin boluses (relative hyperinsulinemia), consider 0.5-1.0 g of carbohydrates/kg per hour of exercise ( $\sim$ 30–60 g), which is similar to carbohydrate requirements to optimize performance in athletes without type 1 diabetes (22-24).

In addition, obesity is as common in children and adolescents with type 1 diabetes as in those without diabetes. It is associated with a higher frequency of cardiovascular risk factors, and it disproportionately affects racial/ethnic minorities in the U.S. (25-29). Therefore, diabetes care providers should monitor weight status and encourage a healthy diet, exercise, and healthy weight as key components of pediatric type 1 diabetes care.

#### School and Child Care

As a large portion of a child's day is spent in school and/or day care, training of school or day care personnel to provide care in accordance with the child's individualized diabetes medical management plan is essential for optimal diabetes management and safe access to all school or day care-sponsored opportunities (10,11,30). In addition, federal and state laws require schools, day care facilities, and other entities to provide needed diabetes care to enable the child to safely access the school or day care environment. Refer to the ADA position statements "Diabetes Care in the School Setting" (10) and "Care of Young Children With Diabetes in the Child Care Setting" (11) and ADA's Safe at School website (www.diabetes.org/resources/

know-your-rights/safe-at-school-statelaws) for additional details.

#### **Psychosocial Issues**

- 14.9 At diagnosis and during routine follow-up care, assess psychosocial issues and family stresses that could impact diabetes management and provide appropriate referrals to trained mental health professionals, preferably experienced in childhood diabetes. E
- 14.10 Mental health professionals should be considered integral members of the pediatric diabetes multidisciplinary team. E
- **14.11** Encourage developmentally appropriate family involvement in diabetes management tasks for children and adolescents, recognizing that premature transfer of diabetes care responsibility to the youth can result in diabetes burnout, suboptimal diabetes management, and deterioration in glycemic control. A
- 14.12 Providers should assess food security, housing stability/ homelessness, health literacy, financial barriers, and social/ community support and apply that information to treatment decisions. E
- 14.13 Providers should consider asking youth and their parents/ caregivers about social adjustment (peer relationships) and school performance to determine whether further intervention is needed. B
- **14.14** Assess youth with diabetes for psychosocial and diabetes-related distress, generally starting at 7-8 years of age. B
- 14.15 Offer adolescents time by themselves with their care provider(s) starting at age 12 years, or when developmentally appropriate. E
- 14.16 Starting at puberty, preconception counseling should be incorporated into routine diabetes care for all girls of childbearing potential. A

14.17 Begin screening youth with type
1 diabetes for disordered eating
between 10 and 12 years of
age. The Diabetes Eating Problems Survey-Revised (DEPS-R)
is a reliable, valid, and brief
screening tool for identifying
disturbed eating behavior. B

Rapid and dynamic cognitive, developmental, and emotional changes occur during childhood, adolescence, and emerging adulthood. Diabetes management during childhood and adolescence places substantial burdens on the youth and family, necessitating ongoing assessment of psychosocial status, social determinants of health, and diabetes distress in the patient and the parents/caregivers during routine diabetes visits (31-39). It is important to consider the impact of diabetes on quality of life as well as the development of mental health problems related to diabetes distress, fear of hypoglycemia (and hyperglycemia), symptoms of anxiety, disordered eating behaviors and eating disorders, and symptoms of depression (40). Consider assessing youth for diabetes distress, generally starting at 7 or 8 years of age (41). Consider screening for depression and disordered eating behaviors using available screening tools (31,42). Early detection of depression, anxiety, disordered eating, and learning disabilities can facilitate effective treatment options and help minimize adverse effects on diabetes management and disease outcomes (36,41). There are validated tools, such as Problem Areas in Diabetes-Teen (PAID-T) and the parent version (P-PAID-T) (37), that can be used in assessing diabetes-specific distress in youth starting at age 12 years and in their parents/caregivers. Furthermore, the complexities of diabetes management require ongoing parental invol-vement in care throughout childhood with developmentally appropriate family teamwork between the growing child/teen and parent in order to maintain adherence and to prevent deterioration in glycemic control (43,44). As diabetes-specific family conflict is related to poorer adherence and glycemic control, it is appropriate to inquire about such conflict during visits and to either help to negotiate a plan for resolution or refer to an appropriate mental health specialist (45). Monitoring of social adjustment (peer relationships) and school performance can facilitate both well-being and academic achievement (46). Suboptimal glycemic control is a risk factor for underperformance at school and increased absenteeism (47).

Shared decision-making with youth regarding the adoption of regimen components and self-management behaviors can improve diabetes self-efficacy, adherence, and metabolic outcomes (26,48). Although cognitive abilities vary, the ethical position often adopted is the "mature minor rule," whereby children after age 12 or 13 years who appear to be "mature" have the right to consent or withhold consent to general medical treatment, except in cases in which refusal would significantly endanger health (49).

Beginning at the onset of puberty or at diagnosis of diabetes, all adolescent females with childbearing potential should receive education about the risks of malformations associated with poor metabolic control and the use of effective contraception to prevent unplanned pregnancy. Preconception counseling using developmentally appropriate educational tools enables adolescent girls to make well-informed decisions (50). Preconception counseling resources tailored for adolescents are available at no cost through the ADA (51). Refer to the ADA position statement "Psychosocial Care for People With Diabetes" for further details (41).

Youth with type 1 diabetes have an increased risk of disordered eating behavior as well as clinical eating disorders with serious short-term and long-term negative effects on diabetes outcomes and health in general. It is important to recognize the unique and dangerous disordered eating behavior of insulin omission for weight control in type 1 diabetes (52) using tools such as the Diabetes Eating Problems Survey-Revised (DEPS-R) to allow for early diagnosis and intervention (42,53–55).

The presence of a mental health professional on pediatric multidisciplinary teams highlights the importance of attending to the psychosocial issues of diabetes. These psychosocial factors are significantly related to self-management difficulties, suboptimal glycemic control, reduced quality of life, and

higher rates of acute and chronic diabetes complications.

# Glycemic Monitoring, Insulin Delivery, and Targets

- 14.18 All children and adolescents with type 1 diabetes should monitor glucose levels multiple times daily (up to 6–10 times/day by blood glucose meter or continuous glucose monitoring), including prior to meals and snacks, at bedtime, and as needed for safety in specific situations such as exercise, driving, or the presence of symptoms of hypoglycemia. B
- 14.19 Real-time continuous glucose monitoring B or intermittently scanned continuous glucose monitoring E should be offered for diabetes management in youth with diabetes on multiple daily injections or insulin pump therapy who are capable of using the device safely (either by themselves or with caregivers). The choice of device should be made based on patient circumstances, desires, and needs.
- 14.20 Automated insulin delivery systems should be offered for diabetes management to youth with type 1 diabetes who are capable of using the device safely (either by themselves or with caregivers). The choice of device should be made based on patient circumstances, desires, and needs. A
- 14.21 Insulin pump therapy alone should be offered for diabetes management to youth on multiple daily injections with type 1 diabetes who are capable of using the device safely (either by themselves or with caregivers). The choice of device should be made based on patient circumstances, desires, and needs. A
- 14.22 Students must be supported at school in the use of diabetes technology, including continuous glucose monitors, insulin pumps, connected

- insulin pens, and automated insulin delivery systems as prescribed by their diabetes care team. E
- 14.23 A1C goals must be individualized and reassessed over time. An A1C of <7% (53 mmol/ mol) is appropriate for many children. B
- 14.24 Less stringent A1C goals (such as <7.5% [58 mmol/mol]) may be appropriate for patients who cannot articulate symptoms of hypoglycemia; have hypoglycemia unawareness; lack access to analog insulins, advanced insulin delivery technology, and/or continuous glucose monitoring; cannot check blood glucose regularly; or have nonglycemic factors that increase A1C (e.g., high glycators). B
- 14.25 Even less stringent A1C goals (such as <8% [64 mmol/ mol]) may be appropriate for patients with a history of severe hypoglycemia, limited life expectancy, or where the harms of treatment are greater than the benefits. B
- 14.26 Providers may reasonably suggest more stringent A1C goals (such as <6.5% [48 mmol/ mol]) for selected individual patients if they can be achieved without significant hypoglycemia, negative impacts on wellbeing, or undue burden of care, or in those who have nonglycemic factors that decrease A1C (e.g., lower erythrocyte life span). Lower targets may also be appropriate during the honeymoon phase. B
- 14.27 Continuous glucose monitoring metrics derived from continuous glucose monitor use over the most recent 14 days (or longer for patients with more glycemic variability), including time in range (70-180 mg/dL), time below target (<70 and <54 mg/dL), and time above target (>180 mg/dL)], are recommended to be used in conjunction with A1C whenever possible. E

Current standards for diabetes management reflect the need to minimize hyperglycemia as safely as possible. The Diabetes Control and Complications Trial (DCCT), which did not enroll children <13 years of age, demonstrated that near normalization of blood glucose levels was more difficult to achieve in adolescents than in adults. Nevertheless, the increased use of basal-bolus regimens, insulin pumps, frequent blood glucose monitoring, automated insulin delivery systems, goal setting, and improved patient education has been associated with more children and adolescents reaching the blood glucose targets recommended by the ADA (56-59), particularly in patients of families in which both the parents/ caregivers and the child with diabetes participate jointly to perform the required diabetes-related tasks.

Lower A1C in adolescence and young adulthood is associated with a lower risk and rate of microvascular and macrovascular complications (60-64) and demonstrates the effects of metabolic memory (65-68).

In addition, type 1 diabetes can be associated with adverse effects on cognition during childhood and adolescence (6,69-71), and neurocognitive imaging differences related to hyperglycemia in children provide another motivation for achieving glycemic targets (6). DKA has been shown to cause adverse effects on brain development and function. Additional factors (72-75) that contribute to adverse effects on brain development and function include young age, severe hypoglycemia at <6 years of age, and chronic hyperglycemia (76,77). However, meticulous use of new therapeutic modalities such as rapid- and long-acting insulin analogs, technological advances (e.g., CGM, sensor-augmented pump therapy, and automated insulin delivery systems), and intensive selfmanagement education now make it more feasible to achieve glycemic control while reducing the incidence of severe hypoglycemia (78-90).

In selecting individualized glycemic targets, the long-term health benefits of achieving a lower A1C should be balanced against the risks of hypoglycemia and the developmental burdens of intensive regimens in youth (91). Recent data with newer devices and insulins indicate

that the risk of hypoglycemia with lower A1C is less than it was before (79,92-100). Some data suggest that there could be a threshold where lower A1C is associated with more hypoglycemia (101,102); however, the confidence intervals were large, suggesting great variability. In addition, achieving lower A1C levels is likely facilitated by setting lower A1C targets (103,104). Lower goals may be possible during the "honeymoon" phase of type 1 diabetes. Special consideration should be given to the risk of hypoglycemia in young children (aged <6 years) who are often unable to recognize, articulate, and/or manage hypoglycemia. However, registry data indicate that A1C targets can be achieved in children, including those aged <6 years, without increased risk of severe hypoglycemia (92,103). Recent data have demonstrated that the use of real-time CGM lowered A1C and increased time in range in adolescents and young adults and, in children aged <8 years old, was associated with a lower risk of hypoglycemia (105,106). Please refer to Section 6, "Glycemic Targets" (https://doi.org/ 10.2337/dc22-S006), for more information on glycemic assessment.

A strong relationship exists between the frequency of blood glucose monitoring and glycemic control (80-87, 107.108). Glucose levels for all children and adolescents with type 1 diabetes should be monitored multiple times daily by blood glucose monitoring or CGM. In the U.S., real-time CGM is approved for nonadjunctive use in children aged 2 years and older, and intermittently scanned CGM is approved for nonadjunctive use in children aged 4 years and older. Metrics derived from CGM include percent time in target range, below target range, and above target range (109). While studies indicate a relationship between time in range and A1C (110, 111), it is still uncertain what the ideal target time in range should be for children, and further studies are needed. Please refer to Section 7, "Diabetes Technology" (https://doi.org/10.2337/ dc22-S007), for more information on the use of blood glucose meters, CGM, and insulin pumps. More information on insulin injection technique can be found in Section 9, "Pharmacologic Approaches to Glycemic Treatment" (https://doi.org/ 10.2337/dc22-S009).

# Key Concepts in Setting Glycemic Targets

- Targets should be individualized, and lower targets may be reasonable based on a benefit-risk assessment.
- Blood glucose targets should be modified in children with frequent hypoglycemia or hypoglycemia unawareness.
- Postprandial blood glucose values should be measured when there is a discrepancy between preprandial blood glucose values and A1C levels and to assess preprandial insulin doses in those on basal-bolus or pump regimens.

#### **Autoimmune Conditions**

#### Recommendation

**14.28** Assess for additional autoimmune conditions soon after the diagnosis of type 1 diabetes and if symptoms develop. **B** 

Because of the increased frequency of other autoimmune diseases in type 1 diabetes, screening for thyroid dysfunction and celiac disease should be considered (112–116). Periodic screening in asymptomatic individuals has been recommended, but the optimal frequency of screening is unclear.

Although much less common than thyroid dysfunction and celiac disease. other autoimmune conditions, such as Addison disease (primary adrenal insufficiency), autoimmune hepatitis, autoimmune gastritis, dermatomyositis, and myasthenia gravis, occur more commonly in the population with type 1 diabetes than in the general pediatric population and should be assessed and monitored as clinically indicated. In addition, relatives of patients should be offered testing for islet autoantibodies through research studies (e.g., TrialNet) and national programs for early diagnosis of preclinical type 1 diabetes (stages 1 and 2).

#### Thyroid Disease

#### Recommendations

- 14.29 Consider testing children with type 1 diabetes for antithyroid peroxidase and antithyroglobulin antibodies soon after diagnosis. B
- **14.30** Measure thyroid-stimulating hormone concentrations at diagnosis when clinically

stable or soon after optimizing glycemia. If normal, suggest rechecking every 1–2 years or sooner if the youth has positive thyroid antibodies or develops symptoms or signs suggestive of thyroid dysfunction, thyromegaly, an abnormal growth rate, or unexplained glycemic variability. B

Autoimmune thyroid disease is the most common autoimmune disorder associated with diabetes, occurring in 17-30% of individuals with type 1 diabetes (113,117,118). At the time of diagnosis,  $\sim$ 25% of children with type 1 diabetes have thyroid autoantibodies (119), the presence of which is predictive of thyroid dysfunction-most commonly hypothyroidism, although hyperthyroidism occurs in  $\sim$ 0.5% of patients with type 1 diabetes (120,121). For thyroid autoantibodies, a study from Sweden indicated that antithyroid peroxidase antibodies were more predictive than antithyroglobulin antibodies in multivariate analysis (122). Thyroid function tests may be misleading (euthyroid sick syndrome) if performed at the time of diagnosis owing to the effect of previous hyperglycemia, ketosis or ketoacidosis, weight loss, etc. Therefore, if performed at diagnosis and slightly abnormal, thyroid function tests should be repeated soon after a period of metabolic stability and achievement of glycemic targets. Subclinical hypothyroidism may be associated with an increased risk of symptomatic hypoglycemia (123) and a reduced linear growth rate. Hyperthyroidism alters glucose metabolism and usually causes deterioration of glycemic control.

#### Celiac Disease

#### Recommendations

- 14.31 Screen youth with type 1 diabetes for celiac disease by measuring IgA tissue transglutaminase (tTG) antibodies, with documentation of normal total serum IgA levels, soon after the diagnosis of diabetes, or IgG tTG and deamidated gliadin antibodies if IgA is deficient. B
- **14.32** Repeat screening within 2 years of diabetes diagnosis and then again after 5 years

and consider more frequent screening in youth who have symptoms or a first-degree relative with celiac disease. B

14.33 Individuals with confirmed celiac disease should be placed on a gluten-free diet for treatment and to avoid complications; they should also have a consultation with a dietitian experienced in managing both diabetes and celiac disease. B

Celiac disease is an immune-mediated disorder that occurs with increased frequency in patients with type 1 diabetes (1.6–16.4% of individuals compared with 0.3–1% in the general population) (112,115,116,124–128). Screening patients with type 1 diabetes for celiac disease is further justified by its association with osteoporosis, iron deficiency, growth failure, and potential increased risk of retinopathy and albuminuria (129–132).

Screening for celiac disease includes measuring serum levels of IgA and tissue transglutaminase (tTG) IgA antibodies, or, with IgA deficiency, screening can include measuring tTG IgG antibodies or deamidated gliadin peptide IgG antibodies. Because most cases of celiac disease are diagnosed within the first 5 years after the diagnosis of type 1 diabetes, screening should be considered at the time of diagnosis and repeated at 2 and then 5 years (126) or if clinical symptoms indicate, such as poor growth or increased hypoglycemia (127,129).

Although celiac disease can be diagnosed more than 10 years after diabetes diagnosis, there are insufficient data after 5 years to determine the optimal screening frequency. Measurement of tTG antibody should be considered at other times in patients with symptoms suggestive of celiac disease (126). Monitoring for symptoms should include an assessment of linear growth and weight gain (127,129). A small bowel biopsy in antibody-positive children is recommended to confirm the diagnosis (133). European guidelines on screening for celiac disease in children (not specific to children with type 1 diabetes) suggest that biopsy may not be necessary in symptomatic children with high antibody titers (i.e., greater than 10 times the

upper limit of normal) provided that further testing is performed (verification of endomysial antibody positivity on a separate blood sample). Whether this approach may be appropriate for asymptomatic children in high-risk groups remains an open question, though evidence is emerging (134). It is also advisable to check for celiac disease-associated HLA types in patients who are diagnosed without a small intestinal biopsy. In symptomatic children with type 1 diabetes and confirmed celiac disease, gluten-free diets reduce symptoms and rates of hypoglycemia (135). The challenging dietary restrictions associated with having both type 1 diabetes and celiac disease place a significant burden on individuals. Therefore, a biopsy to confirm the diagnosis of celiac disease is recommended, especially in asymptomatic children, before establishing a diagnosis of celiac disease (136) and endorsing significant dietary changes. A gluten-free diet was beneficial in asymptomatic adults with positive antibodies confirmed by biopsy (137).

#### Management of Cardiovascular Risk Factors

Hypertension Screening

#### Recommendation

14.34 Blood pressure should be measured at every routine visit. In youth with high blood pressure (blood pressure ≥90th percentile for age, sex, and height or, in adolescents aged ≥13 years, blood pressure ≥120/80 mmHg) on three separate measurements, ambulatory blood pressure monitoring should be strongly considered. B

# Hypertension Treatment

# Recommendations

14.35 Treatment of elevated blood pressure (defined as 90th to <95th percentile for age, sex, and height or, in adolescents aged ≥13 years, 120–129/<80 mmHg) is lifestyle modification focused on healthy nutrition, physical activity, sleep, and, if

- appropriate, weight management. C
- 14.36 In addition to lifestyle modification, ACE inhibitors or angiotensin receptor blockers should be started for treatment of confirmed hypertension (defined as blood pressure consistently ≥95th percentile for age, sex, and height or, in adolescents aged ≥13 years,  $\geq$ 130/80 mmHg). Due to the potential teratogenic effects, females should receive reproductive counseling and ACE inhibitors and angiotensin receptor blockers should be avoided in females of childbearing age who are not using reliable contraception. B
- 14.37 The goal of treatment is blood pressure <90th percentile for age, sex, and height or, in adolescents aged ≥13 years, <130/80 mmHg. C

Blood pressure measurements should be performed using the appropriate size cuff with the youth seated and relaxed. Elevated blood pressure should be confirmed on at least three separate days, and ambulatory blood pressure monitoring should be considered. Evaluation should proceed as clinically indicated (138,139). Treatment is generally initiated with an ACE inhibitor, but an angiotensin receptor blocker can be used if the ACE inhibitor is not tolerated (e.g., due to cough) (140).

#### Dyslipidemia Screening

#### Recommendations

14.38 Initial lipid profile should be performed soon after diagnosis, preferably after glycemia has improved and age is ≥2 years. If initial LDL cholesterol is  $\leq 100 \text{ mg/dL}$  (2.6 mmol/L), subsequent testing should be performed at 9-11 years of age. B Initial testing may be done with a nonfasting non-HDL cholesterol level with confirmatory testing with a fasting lipid panel.

14.39 If LDL cholesterol values are within the accepted risk level (<100 mg/dL [2.6 mmol/L]),a lipid profile repeated every 3 years is reasonable. E

#### Dyslipidemia Treatment

#### Recommendations

- 14.40 If lipids are abnormal, initial therapy should consist of optimizing glycemia and medical nutrition therapy to limit the amount of calories from fat to 25-30% and saturated fat to <7%, limit cholesterol to <200 mg/day, avoid trans fats, and aim for  $\sim$ 10% calories from monounsaturated fats. A
- 14.41 After the age of 10 years, addition of a statin may be considered in patients who, despite medical nutrition therapy and lifestyle changes, continue to have LDL cholesterol >160 mg/dL (4.1 mmol/L) or LDL cholesterol >130 mg/dL (3.4 mmol/L) and one or more cardiovascular disease risk factors. E Due to the potential teratogenic effects, females should receive reproductive counseling and statins should be avoided in females of childbearing age who are not using reliable contraception. B
- **14.42** The goal of therapy is an LDL cholesterol value <100 mg/dL (2.6 mmol/L). E

Population-based studies estimate that 14-45% of children with type 1 diabetes have two or more atherosclerotic cardiovascular disease (ASCVD) risk factors (141-143), and the prevalence of cardiovascular disease (CVD) risk factors increase with age (143) and among racial/ ethnic minorities (25), with girls having a higher risk burden than boys (142).

Pathophysiology. The atherosclerotic process begins in childhood, and although ASCVD events are expected to occur during childhood, observations using a variety of methodologies show that youth with type 1 diabetes may have subclinical CVD within the first decade of diagnosis (144-146). Studies of carotid intima-media thick-

ness have yielded inconsistent results (139,140).

Screening. Diabetes predisposes to the development of accelerated arteriosclerosis. Lipid evaluation for these patients contributes to risk assessment and identifies an important proportion of those with dyslipidemia. Therefore, initial screening should be done soon after diagnosis. If the initial screen is normal, subsequent screening may be done at 9-11 years of age, which is a stable time for lipid assessment in children (147). Children with a primary lipid disorder (e.g., familial hyperlipidemia) should be referred to a lipid specialist. Non-HDL cholesterol level has been identified as a significant predictor of the presence of atherosclerosis—as powerful as any other lipoprotein cholesterol measure in children and adolescents. For both children and adults, non-HDL cholesterol level seems to be more predictive of persistent dyslipidemia and, therefore, atherosclerosis and future events than total cholesterol, LDL cholesterol, or HDL cholesterol levels alone. A major advantage of non-HDL cholesterol is that it can be accurately calculated in a nonfasting state and is therefore practical to obtain in clinical practice as a screening test (148). Youth with type 1 diabetes have a high prevalence of lipid abnormalities (141,149).

Even if normal, screening should be repeated within 3 years, as glycemic control and other cardiovascular risk factors can change dramatically during adolescence (150).

Treatment. Pediatric lipid guidelines provide some guidance relevant to children with type 1 diabetes and secondary dyslipidemia (139,147,151,152); however, there are few studies on modifying lipid levels in children with type 1 diabetes. A 6-month trial of dietary counseling produced a significant improvement in lipid levels (153); likewise, a lifestyle intervention trial with 6 months of exercise in adolescents demonstrated improvement in lipid levels (154). Data from the SEARCH for Diabetes in Youth (SEARCH) study show that improved glucose over a 2-year period is associated with a more favorable lipid profile; however, improved glycemia alone will

not normalize lipids in youth with type 1 diabetes and dyslipidemia (150).

Although intervention data are sparse, the American Heart Association categorizes children with type 1 diabetes in the highest tier for cardiovascular risk and recommends both lifestyle and pharmacologic treatment for those with elevated LDL cholesterol levels (152,155). Initial therapy should include a nutrition plan that restricts saturated fat to 7% of total calories and dietary cholesterol to 200 mg/day. Data from randomized clinical trials in children as young as 7 months of age indicate that this diet is safe and does not interfere with normal growth and development (156).

Neither long-term safety nor cardiovascular outcome efficacy of statin therapy has been established for children; however, studies have shown short-term safety equivalent to that seen in adults and efficacy in lowering LDL cholesterol levels in familial hypercholesterolemia or severe hyperlipidemia, improving endothelial function and causing regression of carotid intimal thickening (157,158). Statins are not approved for patients aged <10 years, and statin treatment should generally not be used in children with type 1 diabetes before this age. Statins are contraindicated in pregnancy; therefore, the prevention of unplanned pregnancies is of paramount importance. Statins should be avoided in females of childbearing age who are not using reliable contraception (see Section 15, "Management of Diabetes in Pregnancy," https://doi.org/10.2337/dc22-S015, more information). The multicenter, randomized, placebo-controlled Adolescent Type 1 Diabetes Cardio-Renal Intervention Trial (AdDIT) provides safety data on pharmacologic treatment with an ACE inhibitor and statin in adolescents with type 1 diabetes (139).

#### Smoking

# Recommendations

14.43 Elicit a smoking history at initial and follow-up diabetes visits; discourage smoking in youth who do not smoke and encourage smoking cessation in those who do smoke. A

**14.44** Electronic cigarette use should be discouraged. **A** 

The adverse health effects of smoking are well recognized with respect to future cancer and CVD risk. Despite this, smoking rates are significantly higher among youth with diabetes than among youth without diabetes (159,160). In youth with diabetes, it is important to avoid additional CVD risk factors. Smoking increases the risk of the onset of albuminuria; therefore, smoking avoidance is important to prevent both microvascular and macrovascular complications (147,161). Discouraging cigarette smoking, including electronic cigarettes (162,163), is an important part of routine diabetes care. In light of recent CDC evidence of deaths related to electronic cigarette use (164,165), no individuals should be advised to use electronic cigarettes, either as a way to stop smoking tobacco or as a recreational drug. In younger children, it is important to assess exposure to cigarette smoke in the home because of the adverse effects of secondhand smoke and to discourage youth from ever smoking.

# Microvascular Complications Nephropathy Screening

#### Recommendation

14.45 Annual screening for albuminuria with a random (morning sample preferred to avoid effects of exercise) spot urine sample for albumin-to-creatinine ratio should be considered at puberty or at age >10 years, whichever is earlier, once the child has had diabetes for 5 years. B

#### Nephropathy Treatment

#### Recommendation

14.46 An ACE inhibitor or an angiotensin receptor blocker, titrated to normalization of albumin excretion, may be considered when elevated urinary albumin-to-creatinine ratio (>30 mg/g) is documented (two of three urine samples obtained over a 6-month interval following efforts to improve glycemic control and normalize blood pressure). E Due to the potential teratogenic effects, females should receive reproductive counseling and ACE inhibitors

and angiotensin receptor blockers should be avoided in females of childbearing age who are not using reliable contraception. B

Data from 7,549 participants <20 years of age in the T1D Exchange clinic registry emphasize the importance of good glycemic and blood pressure control, particularly as diabetes duration increases, in order to reduce the risk of diabetic kidney disease. The data also underscore the importance of routine screening to ensure early diagnosis and timely treatment of albuminuria (166). An estimation of glomerular filtration rate (GFR), calculated using GFR estimating equations from the serum creatinine, height, age, and sex (167), should be considered at baseline and repeated as indicated based on clinical status, age, diabetes duration, and therapies. Improved methods are needed to screen for early GFR loss, since estimated GFR is inaccurate at GFR >60 mL/min/1.73 m<sup>2</sup> (167,168). The AdDIT study in adolescents with type 1 diabetes demonstrated the safety of ACE inhibitor treatment, but the treatment did not change the albumin-to-creatinine ratio over the course of the study (139).

# Retinopathy

#### Recommendations

- 14.47 An initial dilated and comprehensive eye examination is recommended once youth have had type 1 diabetes for 3-5 years, provided they are aged ≥11 years or puberty has started, whichever is earlier, B
- 14.48 After the initial examination, repeat dilated and comprehensive eye examination every 2 years. Less frequent examinations, every 4 years, may be acceptable on the advice of an eye care professional and based on risk factor assessment, including a history of A1C <8%. B
- 14.49 Programs that use retinal photography (with remote reading or use of a validated assessment tool) to improve access to diabetic retinopathy screening can be appropriate

screening strategies for diabetic retinopathy. Such programs need to provide pathways for timely referral for a comprehensive eye examination when indicated. E

Retinopathy (like albuminuria) most commonly occurs after the onset of puberty and after 5-10 years of diabetes duration (169). It is currently recognized that there is a low risk of development of vision-threatening retinal lesions prior to 12 years of age (170,171). A 2019 publication based on the follow-up of the DCCT adolescent cohort supports a lower frequency of eve examinations than previously recommended, particularly in adolescents with A1C closer to the target range (172,173). Referrals should be made to eye care professionals with expertise in diabetic retinopathy and experience in counseling pediatric patients and families on the importance of prevention, early detection, and intervention.

#### Neuropathy

#### Recommendation

14.50 Consider an annual comprehensive foot exam at the start of puberty or at age ≥10 years, whichever is earlier, once the youth has had type 1 diabetes for 5 years. B

Diabetic neuropathy rarely occurs in prepubertal children or after only 1-2 years of diabetes (169), although data suggest a prevalence of distal peripheral neuropathy of 7% in 1,734 youth with type 1 diabetes and association with the presence of CVD risk factors (174,175). A comprehensive foot exam, including inspection, palpation of dorsalis pedis and posterior tibial pulses, and determination of proprioception, vibration, and monofilament sensation, should be performed annually along with an assessment of symptoms of neuropathic pain (175). Foot inspection can be performed at each visit to educate youth regarding the importance of foot care (see Section 12, "Retinopathy, Neuropathy, and Foot Care," https://doi.org/ 10.2337/dc22-S012).

#### **TYPE 2 DIABETES**

For information on risk-based screening for type 2 diabetes and prediabetes in children and adolescents, please refer to Section 2, "Classification and Diagnosis of Diabetes" (https://doi.org/10.2337/ dc22-S002). For additional support for these recommendations, see the ADA position statement "Evaluation and Management of Youth-Onset Type 2 Diabetes" (3).

Type 2 diabetes in youth has increased over the past 20 years, and recent estimates suggest an incidence of  $\sim$ 5,000 new cases per year in the U.S. (176). The CDC published projections for type 2 diabetes prevalence using the SEARCH database; assuming a 2.3% annual increase, the prevalence in those under 20 years of age will quadruple in 40 years (177,178).

Evidence suggests that type 2 diabetes in youth is different not only from type 1 diabetes but also from type 2 diabetes in adults and has unique features, such as a more rapidly progressive decline in β-cell function and accelerated development of diabetes complications (3,179). Longterm follow-up data from the Treatment Options for Type 2 Diabetes in Adolescents and Youth (TODAY) study showed that a majority of individuals with type 2 diabetes diagnosed as youth had microvascular complications by young adulthood (180). Type 2 diabetes disproportionately impacts youth of ethnic and racial minorities and can occur in complex psychosocial and cultural environments, which may make it difficult to sustain healthy lifestyle changes and self-management behaviors (26,181-184). Additional risk factors associated with type 2 diabetes in youth include adiposity, family history of diabetes, female sex, and low socioeconomic status (179).

As with type 1 diabetes, youth with type 2 diabetes spend much of the day in school. Therefore, close communication with and the cooperation of school personnel are essential for optimal diabetes management, safety, and maximal academic opportunities.

#### Screening and Diagnosis

#### Recommendations

**14.51** Risk-based screening for prediabetes and/or type 2 diabetes should be considered after the onset of puberty or ≥10 years

of age, whichever occurs earlier, in youth with overweight (BMI ≥85th percentile) or obesity (BMI ≥95th percentile) and who have one or more additional risk factors for diabetes (see **Table 2.4** for evidence grading of other risk factors).

- 14.52 If screening is normal, repeat screening at a minimum of 3year intervals E, or more frequently if BMI is increasing. C
- 14.53 Fasting plasma glucose, 2-h plasma glucose during a 75-g oral glucose tolerance test, and A1C can be used to test for prediabetes or diabetes in children and adolescents. B
- 14.54 Children and adolescents with overweight or obesity in whom the diagnosis of type 2 diabetes is being considered should have a panel of pancreatic autoantibodies tested to exclude the possibility of autoimmune type 1 diabetes. B

In the last decade, the incidence and prevalence of type 2 diabetes in adolescents has increased dramatically, especially in racial and ethnic minority populations (147,185). A few studies suggest oral glucose tolerance tests or fasting plasma glucose values as more suitable diagnostic tests than A1C in the pediatric population, especially among certain ethnicities (186), although fasting glucose alone may overdiagnose diabetes in children (187,188). In addition, many of these studies do not recognize that diabetes diagnostic criteria are based on long-term health outcomes, and validations are not currently available in the pediatric population (189). A recent analysis of National Health and Nutrition Examination Survey (NHANES) data suggests using A1C for screening of high-risk youth (190).

The ADA acknowledges the limited data supporting A1C for diagnosing type 2 diabetes in children and adolescents. Although A1C is not recommended for diagnosis of diabetes in children with cystic fibrosis or symptoms suggestive of acute onset of type 1 diabetes, and only A1C assays without interference are appropriate

for children with hemoglobinopathies, the ADA continues to recommend A1C for diagnosis of type 2 diabetes in this population (191,192).

#### **Diagnostic Challenges**

Given the current obesity epidemic, distinguishing between type 1 and type 2 diabetes in children can be difficult. Overweight and obesity are common in children with type 1 diabetes (27), and diabetes-associated autoantibodies and ketosis may be present in pediatric patients with clinical features of type 2 diabetes (including obesity and acanthosis nigricans) (187). The presence of islet autoantibodies has been associated with faster progression to insulin deficiency (187). At the onset, DKA occurs in  $\sim$ 6% of youth aged 10-19 years with type 2 diabetes (193). Although uncommon, type 2 diabetes has been observed in prepubertal children under the age of 10 years, and thus it should be part of the differential in children with suggestive symptoms (194). Finally, obesity contributes to the development of type 1 diabetes in some individuals (195), which further blurs the lines between diabetes types. However, accurate diagnosis is critical, as treatment regimens, educational approaches, dietary advice, and outcomes differ markedly between patients with the two diagnoses. The significant diagnostic difficulties posed by MODY are discussed in Section 2, "Classification and Diagnosis of Diabetes" (https://doi.org/10.2337/dc22-S002). In addition, there are rare and atypical diabetes cases that represent a challenge for clinicians and researchers.

## Management

Lifestyle Management

# Recommendations

- 14.55 All youth with type 2 diabetes and their families should receive comprehensive diabetes self-management education and support that is specific to youth with type 2 diabetes and is culturally appropriate. B
- 14.56 Youth with overweight/obesity and type 2 diabetes and their families should be provided with developmentally and culturally appropriate comprehensive lifestyle programs that are integrated

- with diabetes management to achieve a 7–10% decrease in excess weight. **C**
- 14.57 Given the necessity of longterm weight management for youth with type 2 diabetes, lifestyle intervention should be based on a chronic care model and offered in the context of diabetes care. E
- 14.58 Youth with prediabetes and type 2 diabetes, like all children and adolescents, should be encouraged to participate in at least 60 min of moderate to vigorous physical activity daily (with muscle and bone strength training at least 3 days/week) B and to decrease sedentary behavior. C
- 14.59 Nutrition for youth with prediabetes and type 2 diabetes, like for all children and adolescents, should focus on healthy eating patterns that emphasize consumption of nutrient-dense, high-quality foods and decreased consumption of calorie-dense, nutrient-poor foods, particularly sugaradded beverages. B

# Glycemic Targets

- 14.60 Blood glucose monitoring should be individualized, taking into consideration the pharmacologic treatment of the patient. E
- 14.61 Real-time continuous glucose monitoring or intermittently scanned coninuous glucose monitoring should be offered for diabetes management in youth with type 2 diabetes on multiple daily injections or continuous subcutaneous insulin infusion who are capable of using the device safely (either by themselves or with a caregiver). The choice of device should be made based on patient circumstances, desires, and needs. E
- **14.62** Glycemic status should be assessed every 3 months. **E**

- 14.63 A reasonable A1C target for most children and adolescents with type 2 diabetes is <7% (53 mmol/mol). More stringent A1C targets (such as <6.5% [48 mmol/mol]) may be appropriate for selected individual patients if they can be achieved without significant hypoglycemia or other adverse effects of treatment. Appropriate patients might include those with a short duration of diabetes and lesser degrees of β-cell dysfunction and patients treated with lifestyle or metformin only who achieve significant weight improvement. E
- 14.64 Less stringent A1C goals (such as 7.5% [58 mmol/mol]) may be appropriate if there is an increased risk of hypoglycemia. E
- 14.65 A1C targets for patients on insulin should be individualized, taking into account the relatively low rates of hypoglycemia in youth-onset type 2 diabetes. E

#### Pharmacologic Management

#### Recommendations

- 14.66 Initiate pharmacologic therapy, in addition to behavioral counseling for healthful nutrition and physical activity changes, at diagnosis of type 2 diabetes. A
- 14.67 In incidentally diagnosed or metabolically stable patients (A1C <8.5% [69 mmol/mol] and asymptomatic), metformin is the initial pharmacologic treatment of choice if renal function is normal. A
- 14.68 Youth with marked hyperglycemia (blood glucose ≥250 mg/dL [13.9 mmol/L], A1C ≥8.5% [69 mmol/mol]) without acidosis at diagnosis who are symptomatic with polyuria, polydipsia, nocturia, and/or weight loss should be treated initially with basal insulin while metformin is initiated and titrated. B
- 14.69 In patients with ketosis/ ketoacidosis, treatment with subcutaneous or intravenous

- insulin should be initiated to rapidly correct the hyperglycemia and the metabolic derangement. Once acidosis is resolved, metformin should be initiated while subcutaneous insulin therapy is continued. A
- 14.70 In individuals presenting with severe hyperglycemia (blood glucose ≥600 mg/dL [33.3 mmol/L]), consider assessment for hyperglycemic hyperosmolar nonketotic syndrome. A
- 14.71 If glycemic targets are no longer met with metformin (with or without basal insulin), glucagon-like peptide 1 receptor agonist therapy approved for youth with type 2 diabetes should be considered in children 10 years of age or older if they have no past medical history or family history of medullary thyroid carcinoma or multiple endocrine neoplasia type 2. A
- 14.72 Patients treated with metformin, a glucagon-like peptide 1 receptor agonist, and basal insulin who do not meet glycemic targets should be moved to multiple daily injections with basal and premeal bolus insulins or insulin pump therapy. E
- 14.73 In patients initially treated with insulin and metformin who are meeting glucose targets based on blood glucose monitoring, insulin can be tapered over 2-6 weeks by decreasing the insulin dose 10-30% every few days. B
- 14.74 Use of medications not approved by the U.S. Food and Drug Administration for youth with type 2 diabetes is not recommended outside of research trials. B

Treatment of youth-onset type 2 diabetes should include lifestyle management, diabetes self-management education, and pharmacologic treatment. Initial treatment of youth with obesity and diabetes must take into account that diabetes type is often uncertain in the first few weeks of treatment due to overlap

in presentation and that a substantial percentage of youth with type 2 diabetes will present with clinically significant ketoacidosis (196). Therefore, initial therapy should address the hyperglycemia and associated metabolic derangements irrespective of ultimate diabetes type, with adjustment of therapy once metabolic compensation has been established and subsequent information, such as islet autoantibody results, becomes available. Fig. 14.1 provides an approach to the initial treatment of new-onset diabetes in youth with overweight or obesity with clinical suspicion of type 2 diabetes.

Glycemic targets should be individualized, taking into consideration the longterm health benefits of more stringent targets and risk for adverse effects, such as hypoglycemia. A lower target A1C in youth with type 2 diabetes when compared with those recommended in type 1 diabetes is justified by a lower risk of hypoglycemia and higher risk of complications (180,197-200).

Self-management in pediatric diabetes involves both the youth and their parents/adult caregivers. Patients and their families should receive counseling for healthful nutrition and physical activity changes such as eating a balanced diet, achieving and maintaining a healthy weight, and exercising regularly. Physical activity should include aerobic, muscle-strengthening, and bone-strengthening activities (17). A family-centered approach to nutrition and lifestyle modification is essential in children and adolescents with type 2 diabetes, and nutrition recommendations should be culturally appropriate and sensitive to family resources (see Section 5, "Facilitating Behavior Change and Well-being to Improve Health Outcomes," https://doi .org/10.2337/dc22-S005). Given the complex social and environmental context surrounding youth with type 2 diabetes, individual-level lifestyle interventions may not be sufficient to target the complex interplay of family dynamics, mental health, community readiness, and the broader environmental system

A multidisciplinary diabetes team, including a physician, diabetes care and education specialist, registered dietitian nutritionist, and psychologist or social worker, is essential. In addition to achieving glycemic targets and self-management

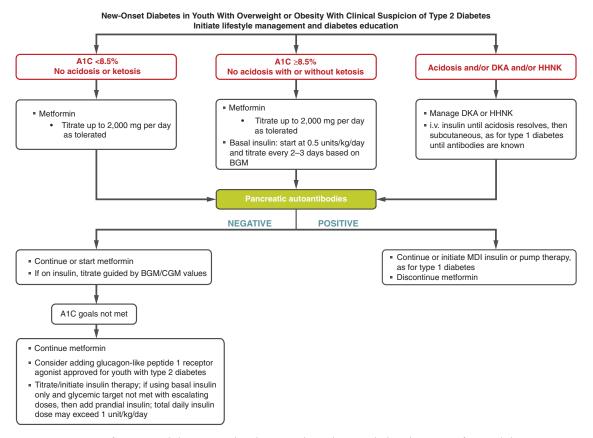


Figure 14.1—Management of new-onset diabetes in youth with overweight or obesity with clinical suspicion of type 2 diabetes. A1C 8.5% = 69 mmol/mol. Adapted from the ADA position statement "Evaluation and Management of Youth-Onset Type 2 Diabetes" (3). BGM, blood glucose monitoring; CGM, continuous glucose monitoring; DKA, diabetic ketoacidosis; HHNK, hyperosmolar hyperglycemic nonketotic syndrome; MDI, multiple daily injections.

education (201–203), initial treatment must include management of comorbidities such as obesity, dyslipidemia, hypertension, and microvascular complications.

Current pharmacologic treatment options for youth-onset type 2 diabetes are limited to three approved drugs classes: insulin, metformin, and glucagonlike peptide 1 receptor agonists. Presentation with ketoacidosis or marked ketosis requires a period of insulin therapy until fasting and postprandial glycemia have been restored to normal or near-normal levels. Insulin pump therapy may be considered as an option for those on longterm multiple daily injections who are able to safely manage the device. Initial treatment should also be with insulin when the distinction between type 1 diabetes and type 2 diabetes is unclear and in patients who have random blood glucose concentrations ≥250 mg/dL (13.9 mmol/L) and/or A1C ≥8.5% (69 mmol/ mol) (204). Metformin therapy should be added after resolution of ketosis/ ketoacidosis.

When initial insulin treatment is not required, initiation of metformin is recommended. The TODAY study found that metformin alone provided durable glycemic control (A1C  $\leq$ 8% [64 mmol/mol] for 6 months) in approximately half of the subjects (205). The Restoring Insulin Secretion (RISE) Consortium study did not demonstrate differences in measures of glucose or  $\beta$ -cell function preservation between metformin and insulin, but there was more weight gain with insulin (206).

To date, the TODAY study is the only trial combining lifestyle and metformin therapy in youth with type 2 diabetes; the combination did not perform better than metformin alone in achieving durable glycemic control (205).

A randomized clinical trial in youth aged 10–17 years with type 2 diabetes demonstrated the addition of subcutaneous liraglutide (up to 1.8 mg daily) to metformin (with or without basal insulin) as safe and effective to decrease A1C (estimated decrease of 1.06 percentage points at 26 weeks and 1.30 at 52

weeks), although it did increase the frequency of gastrointestinal side effects (207). Liraglutide and once-weekly exenatide extended release are approved for the treatment of type 2 diabetes in youth aged 10 years or older (208,209).

Home blood glucose monitoring regimens should be individualized, taking into consideration the pharmacologic treatment of the patient. Although data on CGM in youth with type 2 diabetes are sparse (210), CGM could be considered in individuals requiring frequent blood glucose monitoring for diabetes management.

#### Metabolic Surgery

#### Recommendations

14.75 Metabolic surgery may be considered for the treatment of adolescents with type 2 diabetes who have severe obesity (BMI >35 kg/m²) and who have uncontrolled glycemia and/or serious comorbidities despite lifestyle and pharmacologic intervention. A

14.76 Metabolic surgery should be performed only by an experienced surgeon working as part of a well-organized and engaged multidisciplinary team, including a surgeon, endocrinologist, dietitian nutritionist, behavioral health specialist, and nurse. A

The results of weight loss and lifestyle interventions for obesity in children and adolescents have been disappointing, and treatment options are limited. As an adjunct to lifestyle therapy, liraglutide (3.0 mg) was recently approved for adolescents aged 12 to 17 years with a body weight of at least 60 kg and an initial BMI corresponding to  $\geq$ 30 kg/m<sup>2</sup> for adults (211,212). Over the last decade, weight loss surgery has been increasingly performed in adolescents with obesity. Small retrospective analyses and a prospective multicenter, nonrandomized study suggest that bariatric or metabolic surgery may have benefits in adolescents with obesity and type 2 diabetes similar to those observed in adults. Teenagers experience similar degrees of weight loss, diabetes remission, and improvement of cardiometabolic risk factors for at least 3 years after surgery (213). A secondary data analysis from the Teen-Longitudinal Assessment of Bariatric Surgery (Teen-LABS) and TODAY studies suggests surgical treatment of adolescents with severe obesity and type 2 diabetes is associated with improved glycemic control (214); however, no randomized trials have yet compared the effectiveness and safety of surgery to those of conventional treatment options in adolescents (215). The guidelines used as an indication for metabolic surgery in adolescents generally include BMI >35 kg/m<sup>2</sup> with comorbidities or BMI >40 kg/m<sup>2</sup> with or without comorbidities (216-227). A number of groups, including the Pediatric Bariatric Study Group and Teen-LABS study, have demonstrated the effectiveness of metabolic surgery in adolescents (220-226).

# Prevention and Management of **Diabetes Complications**

Hypertension

#### Recommendations

14.77 Blood pressure should be measured at every visit. In

- youth with high blood pressure (blood pressure ≥90th percentile for age, sex, and height or, in adolescents aged ≥13 years, ≥120/80 mmHg) on three separate measurements, ambulatory blood pressure monitoring should be strongly considered. B
- 14.78 Treatment of elevated blood pressure (defined as 90th to <95th percentile for age, sex, and height or, in adolescents aged ≥13 years, 120-129/<80 mmHg) is lifestyle modification focused on healthy nutrition, physical activity, sleep, and, if appropriate, weight management. C
- 14.79 In addition to lifestyle modification, ACE inhibitors or angiotensin receptor blockers should be started for treatment of confirmed hypertension (defined as blood pressure consistently ≥95th percentile for age, sex, and height or, in adolescents aged ≥13 years, ≥130/80 mmHg). Due to the potential teratogenic effects, females should receive reproductive counseling and ACE inhibitors and angiotensin receptor blockers should be avoided in females of childbearing age who are not using reliable contraception. B
- 14.80 The goal of treatment is blood pressure <90th percentile for age, sex, and height or, in adolescents aged ≥13 years, <130/80 mmHg. C

# Nephropathy

#### Recommendations

- 14.81 Protein intake should be at the recommended daily allowance of 0.8 g/kg/day. E
- **14.82** Urine albumin-to-creatinine ratio should be obtained at the time of diagnosis and annually thereafter. An elevated urine albumin-to-creatinine ratio (>30 mg/g creatinine) should be confirmed on two of three samples. B

- **14.83** Estimated glomerular filtration rate should be determined at the time of diagnosis and annually thereafter. E
- 14.84 In patients with diabetes and hypertension, either an ACE inhibitor or an angiotensin receptor blocker is recommended for those with modestly elevated urinary albuminto-creatinine ratio (30-299 mg/g creatinine) and strongly recommended those with urinary albumin-tocreatinine ratio >300 mg/g creatinine and/or estimated glomerular filtration rate <60 mL/min/1.73 m<sup>2</sup>. E Due to the potential teratogenic effects, females should receive reproductive counseling and ACE inhibitors and angiotensin receptor blockers should be avoided in females of childbearing age who are not using reliable contraception. B
- 14.85 For those with nephropathy, continued monitoring (yearly urinary albumin-to-creatinine ratio, estimated glomerular filtration rate, and serum potassium) may aid in assessing adherence and detecting progression of disease. E
- 14.86 Referral to nephrology is recommended in case of uncertainty of etiology, worsening urinary albumin-to-creatinine ratio, or decrease in estimated glomerular filtration rate. E

# Neuropathy

- 14.87 Youth with type 2 diabetes should be screened for the presence of neuropathy by foot examination at diagnosis and annually. The examination should include inspection, assessment of foot pulses, pinprick and 10-g monofilament sensation tests, testing of vibration sensation using a 128-Hz tuning fork, and ankle reflex tests. C
- 14.88 Prevention should focus on achieving glycemic targets. C

#### Retinopathy

#### Recommendations

- **14.89** Screening for retinopathy should be performed by dilated fundoscopy at or soon after diagnosis and annually thereafter. C
- **14.90** Optimizing glycemia is recommended to decrease the risk or slow the progression of retinopathy. **B**
- 14.91 Less frequent examination (every2 years) may be considered if achieving glycemic targets and a normal eye exam. C
- 14.92 Programs that use retinal photography (with remote reading or use of a validated assessment tool) to improve access to diabetic retinopathy screening can be appropriate screening strategies for diabetic retinopathy. Such programs need to provide pathways for timely referral for a comprehensive eye examination when indicated. E

#### Nonalcoholic Fatty Liver Disease

#### Recommendations

- 14.93 Evaluation for nonalcoholic fatty liver disease (by measuring AST and ALT) should be done at diagnosis and annually thereafter. B
- **14.94** Referral to gastroenterology should be considered for persistently elevated or worsening transaminases. **B**

#### **Obstructive Sleep Apnea**

# Recommendation

14.95 Screening for symptoms of sleep apnea should be done at each visit, and referral to a pediatric sleep specialist for evaluation and a polysomnogram, if indicated, is recommended. Obstructive sleep apnea should be treated when documented. B

# Polycystic Ovary Syndrome

## Recommendations

**14.96** Evaluate for polycystic ovary syndrome in female adolescents with type 2 diabetes, including

- laboratory studies when indicated. **B**
- 14.97 Oral contraceptive pills for treatment of polycystic ovary syndrome are not contraindicated for girls with type 2 diabetes. C
- 14.98 Metformin in addition to lifestyle modification is likely to improve the menstrual cyclicity and hyperandrogenism in girls with type 2 diabetes. E

#### Cardiovascular Disease

#### Recommendation

14.99 Intensive lifestyle interventions focusing on weight loss, dyslipidemia, hypertension, and dysglycemia are important to prevent overt macrovascular disease in early adulthood. E

#### Dyslipidemia

#### Recommendations

- **14.100** Lipid screening should be performed initially after optimizing glycemia and annually thereafter. **B**
- 14.101 Optimal goals are LDL cholesterol <100 mg/dL (2.6 mmol/L), HDL cholesterol >35 mg/dL (0.91 mmol/L), and triglycerides <150 mg/dL (1.7 mmol/L). E
- 14.102 If lipids are abnormal, initial therapy should consist of optimizing glucose control and medical nutritional therapy to limit the amount of calories from fat to 25-30% and saturated fat to <7%, limit cholesterol to <200 mg/day, avoid trans fats, and aim for  $\sim$ 10% calories from monounsaturated fats for elevated LDL. For elevated triglycerides, medical nutrition therapy should also focus on decreasing simple sugar intake and increasing dietary n-3 fatty acids in addition to the above changes. A
- $\begin{array}{lll} \textbf{14.103} & \text{If LDL cholesterol remains} \\ > & 130 \text{ mg/dL after 6 months} \\ \text{of dietary intervention, initiate therapy with statin,} \\ \text{with a goal of LDL} & < & 100 \\ \end{array}$

mg/dL. Due to the potential teratogenic effects, females should receive reproductive counseling and statins should be avoided in females of childbearing age who are not using reliable contraception. B

14.104 If triglycerides are >400 mg/dL (4.7 mmol/L) fasting or >1,000 mg/dL (11.6 mmol/L) nonfasting, optimize glycemia and begin fibrate, with a goal of <400 mg/dL (4.7 mmol/L) fasting (to reduce risk for pancreatitis). C

#### Cardiac Function Testing

#### Recommendation

14.105 Routine screening for heart disease with electrocardiogram, echocardiogram, or stress testing is not recommended in asymptomatic youth with type 2 diabetes. B

Comorbidities may already be present at the time of diagnosis of type 2 diabetes in youth (179,228). Therefore, blood pressure measurement, a fasting lipid panel, assessment of random urine albumin-to-creatinine ratio, and a dilated eye examination should be performed at diagnosis. Additional medical conditions that may need to be addressed include polycystic ovary disease and other comorbidities associated with pediatric obesity, such as sleep apnea, hepatic steatosis, orthopedic complications, and psychosocial concerns. ADA The position statement "Evaluation and Management of Youth-Onset Type 2 Diabetes" (3) provides guidance on the prevention, screening, and treatment of type 2 diabetes and its comorbidities in children and adolescents.

Youth-onset type 2 diabetes is associated with significant microvascular and macrovascular risk burden and a substantial increase in the risk of cardiovascular morbidity and mortality at an earlier age than in those diagnosed later in life (180,229). The higher complication risk in earlier-onset type 2 diabetes is likely related to prolonged lifetime exposure to hyperglycemia and other

atherogenic risk factors, including insulin resistance, dyslipidemia, hypertension, and chronic inflammation. There is a low risk of hypoglycemia in youth with type 2 diabetes, even if they are being treated with insulin (230), and there are high rates of complications (197-200). These diabetes comorbidities also appear to be higher than in youth with type 1 diabetes despite shorter diabetes duration and lower A1C (228). In addition, the progression of vascular abnormalities appears to be more pronounced in youth-onset type 2 diabetes compared with type 1 diabetes of similar duration, including ischemic heart disease and stroke (231).

#### Psychosocial Factors

#### Recommendations

- 14.106 Providers should assess food security, housing stability/ homelessness, health literacy, financial barriers, and social/community support and apply that information to treatment decisions. E
- 14.107 Use patient-appropriate standardized and validated tools to assess for diabetes distress and mental/behavioral health in youth with type 2 diabetes, with attention to symptoms of depression and disordered eating, and refer to specialty care when indicated. B
- 14.108 When choosing glucose-lowering or other medications for youth with overweight or obesity and type 2 diabetes, medication-taking consider behavior and the medications' effect on weight. E
- 14.109 Starting at puberty, preconception counseling should be incorporated into routine diabetes clinic visits for all females of childbearing potential because of the adverse pregnancy outcomes in this population. A
- 14.110 Patients should be screened for tobacco, electronic cigarettes, and alcohol use at diagnosis and regularly thereafter. C

Most youth with type 2 diabetes come from racial/ethnic minority groups,

have low socioeconomic status, and often experience multiple psychosocial stressors (26,41,181-184). Consideration of the sociocultural context and efforts to personalize diabetes management are of critical importance to minimize barriers to care, enhance adherence, and maximize response to treatment.

Evidence about psychiatric disorders and symptoms in youth with type 2 diabetes is limited (232-236), but given the sociocultural context for many youth and the medical burden and obesity associated with type 2 diabetes, ongoing surveillance of mental health/behavioral health is indicated. Symptoms of depression and disordered eating are common and associated with poorer glycemic control (233,237,238).

Many of the medications prescribed for diabetes and psychiatric disorders are associated with weight gain and can increase patients' concerns about eating, body shape, and weight (239,240).

The TODAY study documented (241) that despite disease- and agespecific counseling, 10.2% of the females in the cohort became pregnant over an average of 3.8 years of study participation. Of note, 26.4% of pregnancies ended in a miscarriage, stillbirth, or intrauterine death, and 20.5% of the liveborn infants had a major congenital anomaly.

# TRANSITION FROM PEDIATRIC TO ADULT CARE

#### Recommendations

- 14.111 Pediatric diabetes providers should begin to prepare youth for transition to adult health care in early adolescence and, at the latest, at least 1 year before the transition. E
- 14.112 Both pediatric and adult diabetes care providers should provide support and resources for transitioning young adults. E
- 14.113 Youth with type 2 diabetes should be transferred to an adult-oriented diabetes specialist when deemed appropriate by the patient and provider. E

Care and close supervision of diabetes management are increasingly shifted from parents and other adults to the youth with type 1 or type 2 diabetes throughout childhood and adolescence. The shift from pediatric to adult health care providers, however, often occurs abruptly as the older teen enters the next developmental stage, referred to as emerging adulthood (242), which is a critical period for young people who have diabetes. During this period of major life transitions, youth begin to move out of their parents' homes and must become fully responsible for their diabetes care. Their new responsibilities include self-management of their diabetes, making medical appointments, and financing health care, once they are no longer covered by their parents' health insurance plans (ongoing coverage until age 26 years is currently available under provisions of the U.S. Affordable Care Act). In addition to lapses in health care, this is also a period associated with deterioration in glycemic stability; increased occurrence of acute complications; psychosocial, emotional, and behavioral challenges; and the emergence of chronic complications (243-248). The transition period from pediatric to adult care is prone to fragmentation in health care delivery, which may adversely impact health care quality, cost, and outcomes (249). Worsening diabetes health outcomes during the transition to adult care and early adulthood have been documented (250,251).

Although scientific evidence is limited, it is clear that comprehensive and coordinated planning that begins in early adolescence is necessary to facilitate a seamless transition from pediatric to adult health care (243,244,252,253). New technologies and other interventions are being tried to support the transition to adult care in young adulthood (254-258). A comprehensive discussion regarding the challenges faced during this period, including specific recommendations, is found in the ADA position statement "Diabetes Care for Emerging Adults: Recommendations for Transition From Pediatric to Adult Diabetes Care Systems" (244).

The Endocrine Society, in collaboration with the ADA and other organizations, has developed transition tools for clinicians and youth and families (253).

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