

S23

3. Foundations of Care and Comprehensive Medical Evaluation

Diabetes Care 2016;39(Suppl. 1):S23-S35 | DOI: 10.2337/dc16-S006

The foundations of care include self-management education, nutrition, counseling, physical activity, smoking cessation, immunizations, psychosocial care, and medications (covered in other sections). The comprehensive medical evaluation includes the initial and ongoing evaluations, assessment of complications, management of comorbid conditions, and engagement of the patient throughout the process.

FOUNDATIONS OF CARE

Optimal diabetes management starts with laying down the foundations of care. The health care provider must take a holistic approach in providing care, accounting for all aspects of the patient's life circumstances. A team approach to diabetes management facilitates a comprehensive assessment and development of a plan that addresses the patient's values and circumstances. The investment of time and collaboration can facilitate, and potentially expedite, care delivery and achieve and maintain outcomes.

The initial clinical evaluation should be as comprehensive as possible as the patient will now have to address behavioral, dietary, lifestyle, and pharmaceutical interventions to effectively manage this newly identified chronic condition. The components for the comprehensive medical evaluation (**Table 3.1**) will provide the health care team with information necessary to optimally support a patient with diabetes. In addition to the medical history and physical examination, laboratory tests, nutrition, and psychosocial assessments should be obtained.

Patient Engagement

As discussed in Section 1 "Strategies for Improving Care," the Chronic Care Model (CCM) has been shown to be an effective framework for improving the quality of diabetes care (1–3). This is a patient-centered approach to care that requires a close working relationship between the patient and clinicians involved in care planning and delivery. The foundation of successful diabetes management includes ongoing individual lifestyle and behavioral changes, engagement of the patient, and assessment of the patient's level of understanding about the disease and level of preparedness for self-management.

BASIS FOR INITIAL CARE

Diabetes self-management education (DSME), diabetes self-management support (DSMS), medical nutrition therapy (MNT), counseling on smoking cessation, education on physical activity, guidance on routine immunizations, and psychosocial care are the cornerstone of diabetes management. Patients should be referred for such services if not readily available in the clinical care setting, i.e., referral for DSME, DSMS, MNT, and emotional health concerns. Additionally, specialty and lifestyle change services and programs may be beneficial (**Table 3.2**). Patients should also receive recommended preventive care services (e.g., cancer screening and immunizations); referral for smoking cessation, if needed; and podiatric, ophthalmological, and dental referrals. Clinicians should ensure that individuals with diabetes are screened for complications and comorbidities. Identifying and implementing the initial approach to glycemic control with the patient is one part, not the sole aspect, of the comprehensive care strategy. American Diabetes Association

Suggested citation: American Diabetes Association. Foundations of care and comprehensive medical evaluation. Sec. 3. In Standards of Medical Care in Diabetes—2016. Diabetes Care 2016;39(Suppl. 1):S23–S35

© 2016 by the American Diabetes Association. Readers may use this article as long as the work is properly cited, the use is educational and not for profit, and the work is not altered.

Table 3.1—Components of the comprehensive diabetes medical evaluation Medical history

- Age and characteristics of onset of diabetes (e.g., diabetic ketoacidosis, asymptomatic laboratory finding)
- Eating patterns, nutritional status, weight history, and physical activity habits; nutrition education and behavioral support history and needs
- Presence of common comorbidities, psychosocial problems, and dental disease
- Screen for depression using PHQ-2 (PHQ-9 if PHQ-2 is positive) or Edinburgh Postnatal Depression Scale (EPDS)
- Screen for diabetes distress using DDS or PAID-1
- History of smoking, alcohol consumption, and substance use
- Diabetes education, self-management, and support history and needs
- Review of previous treatment regimens and response to therapy (A1C records)
- Results of glucose monitoring and patient's use of data
- Diabetic ketoacidosis frequency, severity, and cause
- Hypoglycemia episodes, awareness, and frequency and causes
- History of increased blood pressure, increased lipids, and tobacco use
- Microvascular complications: retinopathy, nephropathy, and neuropathy (sensory, including history of foot lesions; autonomic, including sexual dysfunction and gastroparesis)
- Macrovascular complications: coronary heart disease, cerebrovascular disease, and peripheral arterial disease

Physical examination

- Height, weight, and BMI; growth and pubertal development in children and adolescents
- Blood pressure determination, including orthostatic measurements when indicated
- Fundoscopic examination
- Thyroid palpation
- Skin examination (e.g., for acanthosis nigricans, insulin injection or infusion set insertion sites)
- Comprehensive foot examination
 - Inspection
 - Palpation of dorsalis pedis and posterior tibial pulses
 - Presence/absence of patellar and Achilles reflexes
 - Determination of proprioception, vibration, and monofilament sensation

Laboratory evaluation

- A1C, if the results are not available within the past 3 months
- If not performed/available within the past year
 - Fasting lipid profile, including total, LDL, and HDL cholesterol and triglycerides, as needed • Liver function tests
 - Spot urinary albumin-to-creatinine ratio
 - Serum creatinine and estimated glomerular filtration rate
 - Thyroid-stimulating hormone in patients with type 1 diabetes or dyslipidemia or women aged >50 years

ONGOING CARE MANAGEMENT

People with diabetes should receive medical care from a collaborative, integrated team with diabetes expertise. This team may include physicians, nurse practitioners, physician assistants, nurses, dietitians, exercise specialists, pharmacists, dentists, podiatrists, and mental health professionals. Individuals with diabetes must assume an active role in their care.

The patient, family, physician, and other members of the health care team should formulate the management plan. Integral components of the management plan include the foundations of care (DSME, DSMS, MNT, smoking cessation, physical activity, immunizations, and

Table 3.2—Referrals for initial care management

- Eye care professional for annual dilated eye exam
- Family planning for women of reproductive age
- Registered dietitian for MNT
- DSME/DSMS
- Dentist for comprehensive dental and periodontal examination
- Mental health professional, if indicated

psychosocial care). Various strategies and techniques should be used to enable patients to self-manage diabetes, including providing education on problemsolving skills for all aspects of diabetes management. Treatment goals and plans should be individualized and take patient preferences into account. In developing the plan, health care providers should consider the patient's age, school/work schedule and conditions, physical activity, eating patterns, social situation, cultural factors, diabetes complications, health priorities, other medical conditions, preferences for care and selfmanagement, and life expectancy.

DIABETES SELF-MANAGEMENT EDUCATION AND SUPPORT

Recommendations

- In accordance with the national standards for diabetes self-management education (DSME) and support (DSMS), all people with diabetes should participate in DSME to facilitate the knowledge, skills, and ability necessary for diabetes self-care and in DSMS to assist with implementing and sustaining skills and behaviors needed for ongoing self-management, both at diagnosis and as needed thereafter. B
- Effective self-management, improved clinical outcomes, health status, and quality of life are key outcomes of DSME and DSMS and should be measured and monitored as part of care. C
- DSME and DSMS should be patient centered, respectful, and responsive to individual patient preferences, needs, and values, which should guide clinical decisions. A
- DSME and DSMS programs should have the necessary elements in their curricula that are needed to prevent the onset of diabetes.
 DSME and DSMS programs should therefore tailor their content specifically when prevention of diabetes is the desired goal. B
- Because DSME and DSMS can result in cost savings and improved outcomes B, DSME and DSMS should be adequately reimbursed by third-party payers. E

DSME and DSMS are the ongoing processes of facilitating the knowledge,

skills, and ability necessary for diabetes self-care. These processes incorporate the needs, goals, and life experiences of the person with diabetes. The overall objectives of DSME and DSMS are to support informed decision making, self-care behaviors, problem solving, and active collaboration with the health care team to improve clinical outcomes, health status, and quality of life in a cost-effective manner (4).

DSME and DSMS are essential elements of diabetes care (5,6), and the current national standards for DSME and DSMS (4) are based on the evidence of their benefits. Education helps people with diabetes to initiate effective selfmanagement and cope with diabetes when they are first diagnosed. Ongoing DSMS helps people with diabetes to maintain effective self-management throughout a lifetime of diabetes as they face new challenges and as treatment advances become available.

The DSME and DSMS algorithm defines four critical time points for DSME and DSMS delivery (7):

- 1. At diagnosis
- 2. Annually for assessment of education, nutrition, and emotional needs
- When new complicating factors arise that influence self-management
- 4. When transitions in care occur

Current best practice of DSME is a skillbased approach that focuses on helping those with diabetes to make informed self-management choices (4,5). DSME has changed from a didactic approach that focused on providing information to empowerment models that focus on helping those with diabetes to make informed selfmanagement decisions (5). Diabetes care has shifted to an approach that is more patient centered and places the person with diabetes and his or her family at the center of the care model, working in collaboration with health care professionals. Patient-centered care is respectful of and responsive to individual patient preferences, needs, and values. It ensures that patient values guide all decision making (8).

Evidence for the Benefits

Studies have found that DSME is associated with improved diabetes knowledge, improved self-care behaviors (4), lower A1C (6,9,10), lower self-reported weight (11,12), improved quality of life

(10,13), healthy coping (14,15), and lower costs (16,17). Better outcomes were reported for DSME interventions that were longer (>10 h) and included follow-up support (DSMS) (18,19), were culturally (20,21) and age appropriate (22,23), were tailored to individual needs and preferences, and addressed psychosocial issues and incorporated behavioral strategies (5,14,24,25). Both individual and group approaches have been found effective (12,26). There is growing evidence for the role of community health workers (27), as well as peer (27-29) and lay (30) leaders, in providing ongoing support.

DSME is associated with increased primary and preventive service use (16,31,32) and lower acute, inpatient hospital service use (11). Patients who participate in DSME are more likely to follow best practice treatment recommendations, particularly among the Medicare population, and have lower Medicare and insurance claim costs (17,31).

Reimbursement

DSME and DSMS, when provided by a program that meets the national standards (4) and is recognized by the American Diabetes Association (ADA) or other approval bodies, are reimbursed as part of the Medicare program as overseen by the Centers for Medicare & Medicaid Services. DSME is also covered by most health insurance plans. Although DSMS has been shown to be instrumental for improving outcomes and can be provided via phone calls and telehealth, it currently has limited reimbursement as compared with in-person follow-up to DSME.

MEDICAL NUTRITION THERAPY

For many individuals with diabetes, the most challenging part of the treatment plan is determining what to eat. It is the position of the ADA that there is not a one-size-fits-all eating pattern for individuals with diabetes. The ADA recognizes the integral role of MNT in overall diabetes management and recommends that each person with diabetes be actively engaged in self-management, education, and treatment planning with his or her health care team, including the collaborative development of an individualized eating plan (33,34). Therefore, it is important that each member of the health care team be knowledgeable about nutrition therapy principles for people with all types of diabetes and be supportive of their implementation. See **Table 3.3** for specific nutrition recommendations.

Goals of Medical Nutrition Therapy for Adults With Diabetes

- To promote and support healthful eating patterns, emphasizing a variety of nutrient-dense foods in appropriate portion sizes, in order to improve overall health and specifically to
 - Achieve and maintain body weight goals
 - Attain individualized glycemic, blood pressure, and lipid goals
 - Delay or prevent complications of diabetes
- To address individual nutrition needs based on personal and cultural preferences, health literacy and numeracy, access to healthful foods, willingness and ability to make behavioral changes, and barriers to change
- To maintain the pleasure of eating by providing nonjudgmental messages about food choices
- To provide an individual with diabetes with practical tools for developing healthful eating patterns rather than focusing on individual macronutrients, micronutrients, or single foods

MNT is an integral component of diabetes prevention, management, and selfmanagement education. All individuals with diabetes should receive individualized MNT, preferably provided by a registered dietitian who is knowledgeable and skilled in providing diabetes-specific MNT. MNT delivered by a registered dietitian shows A1C decreases of 0.3–1% for people with type 1 diabetes (35–37) and 0.5–2% for people with type 2 diabetes (38–41).

Weight Management

Intensive lifestyle programs with frequent follow-up are required to achieve significant reductions in excess body weight and improve clinical indicators. There is strong and consistent evidence that obesity management can delay progression from prediabetes to type 2 diabetes (42,43) and benefits type 2 diabetes treatment.

In overweight and obese patients with type 2 diabetes, modest weight loss, defined as sustained reduction of 5% of initial body weight, has been shown to improve glycemic control

Торіс	Recommendations	Evidence rating
Effectiveness of nutrition therapy	• An individualized MNT program, preferably provided by a registered dietitian, is recommended for all people with type 1 or type 2 diabetes.	A
	 For people with type 1 diabetes or those with type 2 diabetes who are prescribed a flexible insulin therapy program, education on how to use carbohydrate counting or estimation to determine mealtime insulin dosing can improve glycemic control. 	А
	 For individuals whose daily insulin dosing is fixed, having a consistent pattern of carbohydrate intake with respect to time and amount can result in improved glycemic control and a reduced risk of hypoglycemia. 	В
	• A simple and effective approach to glycemia and weight management emphasizing healthy food choices and portion control may be more helpful for those with type 2 diabetes who are not taking insulin, who have limited health literacy or numeracy, and who are elderly and prone to hypoglycemia.	с
	 Because diabetes nutrition therapy can result in cost savings B and improved outcomes (e.g., A1C reduction) A, MNT should be adequately reimbursed by insurance and other payers. E 	B, A, E
Energy balance	• Modest weight loss achievable by the combination of lifestyle modification and the reduction of energy intake benefits overweight or obese adults with type 2 diabetes and also those at risk for diabetes. Interventional programs to facilitate this process are recommended.	А
Eating patterns and macronutrient distribution	• As there is no single ideal dietary distribution of calories among carbohydrates, fats, and proteins for people with diabetes, macronutrient distribution should be individualized while keeping total calorie and metabolic goals in mind.	E
	 Carbohydrate intake from whole grains, vegetables, fruits, legumes, and dairy products, with an emphasis on foods higher in fiber and lower in glycemic load, should be advised over other sources, especially those containing sugars. 	В
	 People with diabetes and those at risk should avoid sugar-sweetened beverages in order to control weight and reduce their risk for CVD and fatty liver B and should minimize the consumption of sucrose-containing foods that have the capacity to displace healthier, more nutrient-dense food choices. A 	В, А
Protein	 In individuals with type 2 diabetes, ingested protein appears to increase insulin response without increasing plasma glucose concentrations. Therefore, carbohydrate sources high in protein should not be used to treat or prevent hypoglycemia. 	В
Dietary fat	• Whereas data on the ideal total dietary fat content for people with diabetes are inconclusive, an eating plan emphasizing elements of a Mediterranean-style diet rich in monounsaturated fats may improve glucose metabolism and lower CVD risk and can be an effective alternative to a diet low in total fat but relatively high in carbohydrates.	В
	 Eating foods rich in long-chain omega-3 fatty acids, such as fatty fish (EPA and DHA) and nuts and seeds (ALA), is recommended to prevent or treat CVD B; however, evidence does not support a beneficial role for omega-3 dietary supplements. A 	В, А
Micronutrients and herbal supplements	• There is no clear evidence that dietary supplementation with vitamins, minerals, herbs, or spices can improve diabetes, and there may be safety concerns regarding the long-term use of antioxidant supplements such as vitamins E and C and carotene.	C
Alcohol	 Adults with diabetes who drink alcohol should do so in moderation (no more than one drink per day for adult women and no more than two drinks per day for adult men). 	C
	 Alcohol consumption may place people with diabetes at increased risk for delayed hypoglycemia, especially if taking insulin or insulin secretagogues. Education and awareness regarding the recognition and management of delayed hypoglycemia are warranted. 	В
Sodium	 As for the general population, people with diabetes should limit sodium consumption to <2,300 mg/day, although further restriction may be indicated for those with both diabetes and hypertension. 	В

and to reduce the need for glucoselowering medications (44–46). Weight loss can be attained with lifestyle programs that achieve a 500–750 kcal/day energy deficit or provide ~1,200–1,500 kcal/day for women and 1,500–1,800 kcal/day for men, adjusted for the individual's baseline body weight. Although benefits may be seen with as little as 5% weight loss, sustained weight loss of \geq 7% is optimal.

These diets may differ in the types of foods they restrict (such as high-fat or high-carbohydrate foods) but are effective if they create the necessary energy deficit (47–50). The diet choice should be based on the patients' health status and preferences.

Carbohydrates

Studies examining the ideal amount of carbohydrate intake for people with diabetes are inconclusive, although monitoring carbohydrate intake and considering the blood glucose response to dietary carbohydrate are key for improving postprandial glucose control (51,52). The literature concerning glycemic index and glycemic load in individuals with diabetes is complex. Although in some studies lowering the glycemic load of consumed carbohydrates has demonstrated A1C reductions of -0.2% to -0.5% (53,54), a systematic review (53) found that wholegrain consumption was not associated with improvements in glycemic control in type 2 diabetes. One study did find a potential benefit of whole-grain intake in reducing mortality and cardiovascular disease (CVD) among individuals with type 2 diabetes (55). As for all Americans, individuals with diabetes should be encouraged to replace refined carbohydrates and added sugars with whole grains, legumes, vegetables, and fruits. The consumption of sugar-sweetened beverages and "low-fat" or "nonfat" products with high amounts of refined grains and added sugars should be discouraged (56).

Individuals with type 1 or type 2 diabetes taking insulin at mealtimes should be offered intensive education on coupling insulin administration with carbohydrate intake. For people whose meal schedules or carbohydrate consumption is variable, regular counseling to help them to understand the complex relationship between carbohydrate intake and insulin needs, as well as the carbohydrate-counting approach to meal planning, can assist them with effectively modifying insulin dosing from meal to meal and improving glycemic control (36,51,57,58). For individuals on a fixed daily insulin schedule, meal planning should emphasize a relatively fixed carbohydrate consumption pattern with respect to both time and amount (34). By contrast, a simpler diabetes meal planning approach emphasizing portion control and healthful food choices may be better suited for some elderly individuals, those with cognitive dysfunction, and those for whom there are concerns over health literacy and numeracy (34–36,38,51,57).

Protein

For individuals without evidence of diabetic kidney disease, the evidence is inconclusive about recommending an ideal amount of protein for optimizing glycemic control or for improving one or more CVD risk measures (53). Therefore, these goals should be individualized. For those with diabetic kidney disease (with albuminuria, reduced estimated glomerular filtration rate), dietary protein should be maintained at the recommended daily allowance of 0.8 g/kg body weight per day. Reducing the amount of dietary protein below the recommended daily allowance is not recommended because it does not alter glycemic measures, cardiovascular risk measures, or the rate at which glomerular filtration rate declines (59,60). In individuals with type 2 diabetes, ingested protein may enhance the insulin response to dietary carbohydrates (61). Therefore, carbohydrate sources high in protein should not be used to treat or prevent hypoglycemia. The effects of protein intake on blood glucose levels in type 1 diabetes are less clear.

Fats

Limited research exists concerning the ideal amount of fat for individuals with diabetes. The Institute of Medicine has defined an acceptable macronutrient distribution range for all adults for total fat of 20–35% of energy with no tolerable upper intake level defined (62). The type of fatty acids consumed is more important than total amount of fat when looking at metabolic goals and CVD risk (63-65). Multiple randomized controlled trials including patients with type 2 diabetes have reported that a Mediterranean-style eating pattern (63,66-68), rich in monounsaturated fats, can improve both glycemic control and blood lipids. However, a systematic review concluded that dietary supplements with

omega-3 fatty acids did not improve glycemic control in individuals with type 2 diabetes (53). Randomized controlled trials also do not support recommending omega-3 supplements for primary or secondary prevention of CVD (69–73). People with diabetes should be advised to follow the guidelines for the general population for the recommended intakes of saturated fat, dietary cholesterol, and *trans* fat (64). In general, *trans* fats should be avoided.

Sodium

As for the general population, people with diabetes should limit their sodium consumption to <2,300 mg/day. Lowering sodium intake (i.e., 1,500 mg/day) may benefit blood pressure in certain circumstances (74). The American Heart Association recommends 1,500 mg/day for African Americans; people diagnosed with hypertension, diabetes, or chronic kidney disease; and people over 51 years of age (75). However, other studies (76,77) have recommended caution for universal sodium restriction to 1,500 mg in this population. Sodium intake recommendations should take into account palatability, availability, affordability, and the difficulty of achieving low-sodium recommendations in a nutritionally adequate diet (78).

For complete discussion and references of all recommendations, see the ADA position statement "Nutrition Therapy Recommendations for the Management of Adults With Diabetes" (34).

PHYSICAL ACTIVITY

Recommendations

- Children with diabetes or prediabetes should be encouraged to engage in at least 60 min of physical activity each day. B
- Adults with diabetes should be advised to perform at least 150 min/week of moderate-intensity aerobic physical activity (50–70% of maximum heart rate), spread over at least 3 days/week with no more than 2 consecutive days without exercise. A
- All individuals, including those with diabetes, should be encouraged to reduce sedentary time, particularly by breaking up extended amounts of time (>90 min) spent sitting. B
- In the absence of contraindications, adults with type 2 diabetes should be encouraged to perform resistance training at least twice per week. A

Physical activity is a general term that includes all movement that increases energy use and is an important part of the diabetes management plan. Exercise is a more specific form of physical activity that is structured and designed to improve physical fitness. Although both are important, exercise has been shown to improve blood glucose control, reduce cardiovascular risk factors, contribute to weight loss, and improve well-being. Physical activity is as important for those with type 1 diabetes as it is for the general population, but its specific role in preventing diabetes complications and controlling blood glucose is not as clear as it is for those with type 2 diabetes.

Furthermore, regular exercise may prevent type 2 diabetes in high-risk individuals (43,79,80) (see Section 4 "Prevention or Delay of Type 2 Diabetes"). Structured exercise interventions of at least 8 weeks' duration have been shown to lower A1C by an average of 0.66% in people with type 2 diabetes, even with no significant change in BMI (80). There are also considerable data for the health benefits (e.g., increased cardiovascular fitness, muscle strength, improved insulin sensitivity, etc.) of regular exercise for those with type 1 diabetes (81). Higher levels of exercise intensity are associated with greater improvements in A1C and in fitness (82). Other benefits include slowing the decline in mobility among overweight patients with diabetes (83). "Exercise and Type 2 Diabetes: The American College of Sports Medicine and the American **Diabetes Association: Joint Position** Statement" (84) reviews the evidence for the benefits of exercise in people with type 2 diabetes.

Exercise and Children

As is recommended for all children, children with diabetes or prediabetes should be encouraged to engage in at least 60 min of physical activity each day. Included in the 60 min each day, children should engage in vigorous-intensity aerobic activity, muscle-strengthening activities, and bone-strengthening activities at least 3 of those days (85).

Frequency and Type of Physical Activity

The U.S. Department of Health and Human Services' physical activity guidelines for Americans (86) suggest that adults over age 18 years do 150 min/week of moderate-intensity or 75 min/week of vigorous-intensity aerobic physical activity, or an equivalent combination of the two. In addition, the guidelines suggest that adults do muscle-strengthening activities that involve all major muscle groups 2 or more days/week. The guidelines suggest that adults over age 65 years or those with disabilities follow the adult guidelines if possible or, if this is not possible, be as physically active as they are able.

Recent evidence supports that all individuals, including those with diabetes, should be encouraged to reduce the amount of time spent being sedentary (e.g., working at a computer, watching TV), particularly, by breaking up extended amounts of time (>90 min) spent sitting by briefly standing or walking (87).

Physical Activity and Glycemic Control

On the basis of physical activity studies that include people with diabetes, it is reasonable to recommend that people with diabetes will specifically benefit from following the U.S. Department of Health and Human Services' physical activity guidelines. For example, studies included in the meta-analysis of the effects of exercise interventions on glycemic control (80) reported a mean of 3.4 sessions/ week, with a mean of 49 min/session.

Clinical trials have provided strong evidence for the A1C-lowering value of resistance training in older adults with type 2 diabetes (84) and for an additive benefit of combined aerobic and resistance exercise in adults with type 2 diabetes (88,89). If not contraindicated, patients with type 2 diabetes should be encouraged to do at least two weekly sessions of resistance exercise (exercise with free weights or weight machines), with each session consisting of at least one set of five or more different resistance exercises involving the large muscle groups (84).

Pre-exercise Evaluation

As discussed more fully in Section 8 "Cardiovascular Disease and Risk Management," the best protocol for screening asymptomatic patients with diabetes for coronary artery disease remains unclear. The ADA consensus report "Screening for Coronary Artery Disease in Patients With Diabetes" (90) concluded that routine testing is not recommended. Providers should perform a careful history being aware of the atypical presentation of coronary artery disease in patients with diabetes and assess other cardiovascular risk factors. Certainly, high-risk patients should be encouraged to start with short periods of low-intensity exercise and slowly increase the intensity and duration. Providers should assess patients for conditions that might contraindicate certain types of exercise or predispose to injury, such as uncontrolled hypertension, autonomic neuropathy, peripheral neuropathy, a history of foot lesions, and untreated proliferative retinopathy. The patient's age and previous physical activity level should be considered. The provider should customize the exercise regimen to the individual's needs. Those with complications may require a more thorough evaluation (81).

Hypoglycemia

In individuals taking insulin and/or insulin secretagogues, physical activity may cause hypoglycemia if the medication dose or carbohydrate consumption is not altered. Individuals on these therapies may need to ingest some added carbohydrate if pre-exercise glucose levels are <100 mg/dL (5.6 mmol/L), depending on whether they can lower insulin levels during the workout (such as with an insulin pump or reduced preexercise insulin dosage), the time of day exercise is done, and the intensity and duration of the activity. Hypoglycemia is less common in patients with diabetes who are not treated with insulin or insulin secretagogues, and no preventive measures for hypoglycemia are usually advised in these cases. Intense activities may actually raise blood glucose levels instead of lowering them (91).

Exercise in the Presence of Specific Long-term Complications of Diabetes *Retinopathy*

If proliferative diabetic retinopathy or severe nonproliferative diabetic retinopathy is present, then vigorous-intensity aerobic or resistance exercise may be contraindicated because of the risk of triggering vitreous hemorrhage or retinal detachment (92).

Peripheral Neuropathy

Decreased pain sensation and a higher pain threshold in the extremities result in an increased risk of skin breakdown, infection, and Charcot joint destruction with some forms of exercise. Therefore, a thorough assessment should be done to ensure that neuropathy does not alter kinesthetic or proprioceptive sensation during physical activity. Studies have shown that moderateintensity walking may not lead to an increased risk of foot ulcers or reulceration in those with peripheral neuropathy who use proper footwear (93). In addition, 150 min/week of moderate exercise was reported to improve outcomes in patients with milder forms of neuropathy (94). All individuals with peripheral neuropathy should wear proper footwear and examine their feet daily to detect lesions early. Anyone with a foot injury or open sore should be restricted to non-weightbearing activities.

Autonomic Neuropathy

Autonomic neuropathy can increase the risk of exercise-induced injury or adverse events through decreased cardiac responsiveness to exercise, postural hypotension, impaired thermoregulation, impaired night vision due to impaired papillary reaction, and greater susceptibility to hypoglycemia (95). Cardiovascular autonomic neuropathy is also an independent risk factor for cardiovascular death and silent myocardial ischemia (96). Therefore, individuals with diabetic autonomic neuropathy should undergo cardiac investigation before beginning physical activity more intense than that to which they are accustomed.

Albuminuria and Nephropathy

Physical activity can acutely increase urinary protein excretion. However, there is no evidence that vigorous-intensity exercise increases the rate of progression of diabetic kidney disease, and there appears to be no need for specific exercise restrictions for people with diabetic kidney disease (92).

SMOKING CESSATION: TOBACCO AND e-CIGARETTES

Recommendations

- Advise all patients not to use cigarettes, other tobacco products, or e-cigarettes. A
- Include smoking cessation counseling and other forms of treatment as a routine component of diabetes care. B

Results from epidemiological, case-control, and cohort studies provide convincing evidence to support the causal link between cigarette smoking and health risks (97). Other studies of individuals with diabetes consistently demonstrate that smokers (and people exposed to secondhand smoke) have a heightened risk of CVD, premature death, and microvascular complications. Smoking may have a role in the development of type 2 diabetes (98). One study in smokers with newly diagnosed type 2 diabetes found that smoking cessation was associated with amelioration of metabolic parameters and reduced blood pressure and albuminuria at 1 year (99).

The routine and thorough assessment of tobacco use is essential to prevent smoking or encourage cessation. Numerous large randomized clinical trials have demonstrated the efficacy and costeffectiveness of brief counseling in smoking cessation, including the use of telephone quit lines, in reducing tobacco use. For the patient motivated to quit, the addition of pharmacological therapy to counseling is more effective than either treatment alone. Special considerations should include assessment of level of nicotine dependence, which is associated with difficulty in quitting and relapse (100). Although some patients may gain weight in the period shortly after smoking cessation, recent research has demonstrated that this weight gain does not diminish the substantial CVD benefit realized from smoking cessation (101). Nonsmokers should be advised not to use e-cigarettes.

There are no rigorous studies that have demonstrated that e-cigarettes are a healthier alternative to smoking or that e-cigarettes can facilitate smoking cessation. More extensive research of their short- and long-term effects is needed to determine their safety and their cardiopulmonary effects in comparison with smoking and standard approaches to smoking cessation (102–104).

IMMUNIZATION

Recommendations

 Provide routine vaccinations for children and adults with diabetes as for the general population according to age-related recommendations. C

- Administer hepatitis B vaccine to unvaccinated adults with diabetes who are aged 19–59 years. C
- Consider administering hepatitis B vaccine to unvaccinated adults with diabetes who are aged ≥60 years. C

As for the general population, all children and adults with diabetes should receive routine vaccinations (105,106) according to age-specific recommendations (see the **adult vaccination schedule** available from http://www.cdc.gov/ vaccines/schedules/hcp/imz/adult.html and the **child and adolescent vaccination schedule** available from http:// www.cdc.gov/vaccines/schedules/hcp/ imz/child-adolescent.html).

The Centers for Disease Control and Prevention (CDC) Advisory Committee on Immunization Practices recommends influenza and pneumococcal vaccines for all individuals with diabetes (http:// www.cdc.gov/vaccines/schedules).

Influenza

Influenza is a common, preventable infectious disease associated with high mortality and morbidity in vulnerable populations, such as the young and the elderly and people with chronic diseases. Regardless of sex, race, and socioeconomic status, adults with diabetes 25-64 years of age who died are four times more likely to have pneumonia and influenza recorded on their death certificates than adults without diabetes who died at comparable ages (107). In a case-control series, the influenza vaccine was shown to reduce diabetes-related hospital admission by as much as 79% during flu epidemics (108).

Pneumococcal Pneumonia

Like influenza, pneumococcal pneumonia is a common, preventable disease. People with diabetes may be at increased risk for the bacteremic form of pneumococcal infection and have been reported to have a high risk of nosocomial bacteremia, with a mortality rate as high as 50% (109). All patients with diabetes 2 years of age and older should receive the pneumococcal polysaccharide vaccine 23 (PPSV23). There is sufficient evidence to support that people with diabetes have appropriate serologic and clinical responses to these vaccinations. The ADA endorses the CDC advisory panel recommendation that both pneumococcal conjugate vaccine 13 (PCV13) and PPSV23 should be administered routinely in series to all adults aged \geq 65 years.

Hepatitis **B**

Compared with the general population, people with type 1 or type 2 diabetes have higher rates of hepatitis B. This may be due to contact with infected blood or through improper equipment use (glucose monitoring devices or infected needles). Because of the higher likelihood of transmission, hepatitis B vaccine is recommended for adults with diabetes.

PSYCHOSOCIAL ISSUES

Recommendations

- The patient's psychological and social situation should be addressed in the medical management of diabetes. **B**
- Psychosocial screening and followup may include, but are not limited to, attitudes about the illness, expectations for medical management and outcomes, affect/ mood, general and diabetes-related quality of life, resources (financial, social, and emotional), and psychiatric history. E
- Routinely screen for psychosocial problems such as depression, diabetes-related distress, anxiety, eating disorders, and cognitive impairment. B
- Older adults (aged ≥65 years) with diabetes should be considered for evaluation of cognitive function and depression screening and treatment. B
- Patients with comorbid diabetes and depression should receive a stepwise collaborative care approach for the management of depression. A

Emotional well-being is an important part of diabetes care and self-management. Psychological and social problems can impair the individual's (110–112) or family's (113) ability to carry out diabetes care tasks and therefore compromise health status. There are opportunities for the clinician to routinely assess psychosocial status in a timely and efficient manner for referral for appropriate services. A systematic review and meta-analysis showed that psychosocial interventions modestly but significantly improved A1C (standardized mean difference -0.29%) and mental health outcomes. However, there was a limited association between the effects on A1C and mental health, and no intervention characteristics predicted benefit on both outcomes (114).

Screening

Key opportunities for psychosocial screening occur at diabetes diagnosis, during regularly scheduled management visits, during hospitalizations, with new onset of complications, or when problems with glucose control, quality of life, or self-management are identified. Patients are likely to exhibit psychological vulnerability at diagnosis, when their medical status changes (e.g., end of the honeymoon period), when the need for intensified treatment is evident, and when complications are discovered. Depression affects \sim 20–25% of people with diabetes (115). Individuals with both diabetes and major depressive disorder have a twofold increased risk for newonset myocardial infarction compared with either disease state alone (116). There appears to be a bidirectional relationship between both diabetes (117) and metabolic syndrome (118) and depression.

Diabetes Distress

Diabetes-related distress (DD) is distinct from depressive disorders and is very common (119-121) in people with diabetes and their family members (113). DD refers to significant negative psychological reactions related to emotional burdens and worries specific to an individual's experience in having to manage a severe, complicated, and demanding chronic disease such as diabetes (120-122). Its prevalence is reported to be 18-45%, with an incidence of 38-48% over 18 months. High levels of distress are significantly linked to medication nonadherence (122), higher A1C, lower self-efficacy, and poorer dietary and exercise behaviors (15,120). The clinician needs to understand that individuals may fall into one of three categories: those with depression and DD, those

with depression without significant DD, and those with DD without significant depression. Understanding the category in which a particular patient belongs facilitates a customized care approach that may include DSME, DSMS, cognitive therapy, or treatment for depression (psychotherapy and/ or psychotropic medications). The screening of all patients with diabetes with the Patient Health Questionnaire-2 (PHQ-2) and either the Diabetes Distress Scale (DDS) or Problem Areas in Diabetes (PAID)-1 scale can help to facilitate this (24,123,124).

Other issues known to affect selfmanagement and health outcomes include attitudes about the illness, expectations for medical management and outcomes, anxiety, general and diabetesrelated quality of life, resources (financial, social, and emotional) (125), and psychiatric history (126).

Referral to a Mental Health Specialist

Indications for referral to a mental health specialist familiar with diabetes management may include possibility of self-harm, gross disregard for the medical regimen (by self or others) (127), depression, overall stress related to work-life balance, debilitating anxiety (alone or with depression), indications of an eating disorder (128), or cognitive functioning that significantly impairs judgment. It is preferable to incorporate psychological assessment and treatment into routine care rather than waiting for a specific problem or deterioration in metabolic or psychological status (24,119). In the second Diabetes Attitudes, Wishes and Needs (DAWN2) study, significant DD was reported by 45% of the participants, but only 24% reported that their health care team asked them how diabetes affected their life (119).

Although the clinician may not feel qualified to treat psychological problems (129), optimizing the patientprovider relationship as a foundation may increase the likelihood of the patient accepting referral for other services. Collaborative care interventions and a team approach have demonstrated efficacy in diabetes and depression (130,131). Interventions to enhance self-management and address severe distress have demonstrated efficacy in DD (15).

COMPREHENSIVE MEDICAL EVALUATION

Recommendations

A complete medical evaluation should be performed at the initial visit to

- Confirm the diagnosis and classify diabetes. **B**
- Detect diabetes complications and potential comorbid conditions. E
- Review previous treatment and risk factor control in patients with established diabetes. E
- Begin patient engagement in the formulation of a care management plan. B
- Develop a plan for continuing care. **B**

Besides assessing diabetes-related complications and comorbidities, clinicians and their patients need to be aware of other common conditions that affect people with diabetes. Improved disease prevention and treatment mean that people with diabetes are living longer and developing heart failure, fatty liver disease, obstructive sleep apnea, and arthritis—conditions that affect people with diabetes more often than age-matched people without diabetes and that may complicate diabetes management (132–136).

Adults who develop type 1 diabetes may develop additional autoimmune disorders including thyroid or adrenal dysfunction and celiac disease, although the risk of coexisting autoimmunity is lower in adults than for youth with type 1 diabetes. For additional details on autoimmune conditions, see Section 11 "Children and Adolescents."

COMORBIDITIES

Fatty Liver Disease

Elevations of hepatic transaminase concentrations are significantly associated with higher BMI, waist circumference, and triglyceride levels and lower HDL cholesterol levels. In a prospective analysis, diabetes was significantly associated with incident nonalcoholic chronic liver disease and with hepatocellular carcinoma (137). Interventions that improve metabolic abnormalities in patients with diabetes (weight loss, glycemic control, and treatment with specific drugs for hyperglycemia or dyslipidemia) are also beneficial for fatty liver disease (138).

Obstructive Sleep Apnea

Age-adjusted rates of obstructive sleep apnea, a risk factor for CVD, are significantly higher (4- to 10-fold) with obesity, especially with central obesity (139). The prevalence of obstructive sleep apnea in the population with type 2 diabetes may be as high as 23% (140). In obese participants enrolled in the Action for Health in Diabetes (Look AHEAD) trial, it exceeded 80% (141). Sleep apnea treatment significantly improves quality of life and blood pressure control. The evidence for a treatment effect on glycemic control is mixed (142).

Cancer

Diabetes (possibly only type 2 diabetes) is associated with increased risk of cancers of the liver, pancreas, endometrium, colon/rectum, breast, and bladder (143). The association may result from shared risk factors between type 2 diabetes and cancer (older age, obesity, and physical inactivity) but may also be due to hyperinsulinemia or hyperglycemia (144). Patients with diabetes should be encouraged to undergo recommended age- and sex-appropriate cancer screenings and to reduce their modifiable cancer risk factors (smoking, obesity, and physical inactivity).

Fractures

Age-specific hip fracture risk is significantly increased in both type 1 (relative risk 6.3) and type 2 (relative risk 1.7) diabetes in both sexes (145). Type 1 diabetes is associated with osteoporosis, but in type 2 diabetes, an increased risk of hip fracture is seen despite higher bone mineral density (BMD) (146). In three large observational studies of older adults, femoral neck BMD T-score and the World Health Organization Fracture Risk Assessment Tool (FRAX) score were associated with hip and nonspine fractures. Fracture risk was higher in participants with diabetes compared with those without diabetes for a given T-score and age for a given FRAX score (147). Providers should assess fracture history and risk factors in older patients with diabetes and recommend measurement of BMD if appropriate for the patient's age and sex. Fracture prevention strategies for people with diabetes are the same as for the general population and include vitamin D supplementation. For patients with type 2 diabetes with fracture risk factors, thiazolidinediones (148) and sodium–glucose cotransporter 2 inhibitors should be avoided as their use has been associated with a higher risk of fractures (149).

Low Testosterone in Men

Mean levels of testosterone are lower in men with diabetes compared with agematched men without diabetes, but obesity is a major confounder (150). Treatment in asymptomatic men is controversial. The evidence that testosterone replacement affects outcomes is mixed, and recent guidelines do not recommend testing and treating men without symptoms (151).

Periodontal Disease

Periodontal disease is more severe, but not necessarily more prevalent, in patients with diabetes than in those without (152). Current evidence suggests that periodontal disease adversely affects diabetes outcomes, although evidence for treatment benefits remains controversial (136).

Hearing Impairment

Hearing impairment, both in high-frequency and low/mid-frequency ranges, is more common in people with diabetes than in those without, perhaps due to neuropathy and/or vascular disease. In a National Health and Nutrition Examination Survey (NHANES) analysis, hearing impairment was about twice as prevalent in people with diabetes compared with those without, after adjusting for age and other risk factors for hearing impairment (153).

Cognitive Impairment

Diabetes is associated with a significantly increased risk and rate of cognitive decline and an increased risk of dementia (154,155). In a 15-year prospective study of community-dwelling people aged >60 years, the presence of diabetes at baseline significantly increased the age- and sex-adjusted incidence of all-cause dementia, Alzheimer disease, and vascular dementia compared with rates in those with normal glucose tolerance (156). In a substudy of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) clinical trial, there were no differences in cognitive outcomes between the intensive and standard glycemic control

groups, although there was significantly less of a decrement in total brain volume, as measured by MRI, in participants in the intensive arm (157). The effects of hyperglycemia and insulin on the brain are areas of intense research interest.

References

1. Stellefson M, Dipnarine K, Stopka C. The Chronic Care Model and diabetes management in US primary care settings: a systematic review. Prev Chronic Dis 2013;10:E26

 Coleman K, Austin BT, Brach C, Wagner EH.
 Evidence on the Chronic Care Model in the new millennium. Health Aff (Millwood) 2009; 28:75–85

3. Gabbay RA, Bailit MH, Mauger DT, Wagner EH, Siminerio L. Multipayer patient-centered medical home implementation guided by the Chronic Care Model. Jt Comm J Qual Patient Saf 2011;37:265–273

4. Haas L, Maryniuk M, Beck J, et al.; 2012 Standards Revision Task Force. National standards for diabetes self-management education and support. Diabetes Care 2014;37(Suppl. 1): S144–S153

5. Marrero DG, Ard J, Delamater AM, et al. Twenty-first century behavioral medicine: a context for empowering clinicians and patients with diabetes: a consensus report. Diabetes Care 2013;36:463–470

6. Norris SL, Lau J, Smith SJ, Schmid CH, Engelgau MM. Self-management education for adults with type 2 diabetes: a meta-analysis of the effect on glycemic control. Diabetes Care 2002;25:1159–1171

7. Powers MA, Bardsley J, Cypress M, et al. Diabetes self-management education and support in type 2 diabetes: a joint position statement of the American Diabetes Association, the American Association of Diabetes Educators, and the Academy of Nutrition and Dietetics. Diabetes Care 2015;38:1372–1382

8. Committee on Quality of Health Care in America. Institute of Medicine. Crossing the quality chasm: a new health system for the 21st century [Internet], 2001. Available from http://www.iom .edu/Reports/2001/Crossing-the-Quality-Chasm-A-New-Health-System-for-the-21st-Century.aspx. Accessed 1 October 2015

9. Frosch DL, Uy V, Ochoa S, Mangione CM. Evaluation of a behavior support intervention for patients with poorly controlled diabetes. Arch Intern Med 2011;171:2011–2017

10. Cooke D, Bond R, Lawton J, et al.; U.K. NIHR DAFNE Study Group. Structured type 1 diabetes education delivered within routine care: impact on glycemic control and diabetes-specific quality of life. Diabetes Care 2013;36:270–272

11. Steinsbekk A, Rygg LØ, Lisulo M, Rise MB, Fretheim A. Group based diabetes self-management education compared to routine treatment for people with type 2 diabetes mellitus. A systematic review with meta-analysis. BMC Health Serv Res 2012;12:213

12. Deakin T, McShane CE, Cade JE, Williams RDRR. Group based training for self-management strategies in people with type 2 diabetes mellitus. Cochrane Database Syst Rev 2005;2: CD003417

13. Cochran J, Conn VS. Meta-analysis of quality of life outcomes following diabetes selfmanagement training. Diabetes Educ 2008;34: 815–823

14. Thorpe CT, Fahey LE, Johnson H, Deshpande M, Thorpe JM, Fisher EB. Facilitating healthy coping in patients with diabetes: a systematic review. Diabetes Educ 2013;39:33–52

15. Fisher L, Hessler D, Glasgow RE, et al. REDEEM: a pragmatic trial to reduce diabetes distress. Diabetes Care 2013;36:2551–2558

16. Robbins JM, Thatcher GE, Webb DA, Valdmanis VG. Nutritionist visits, diabetes classes, and hospitalization rates and charges: the Urban Diabetes Study. Diabetes Care 2008;31: 655–660

17. Duncan I, Ahmed T, Li QE, et al. Assessing the value of the diabetes educator. Diabetes Educ 2011;37:638–657

18. Piatt GA, Anderson RM, Brooks MM, et al. 3-Year follow-up of clinical and behavioral improvements following a multifaceted diabetes care intervention: results of a randomized controlled trial. Diabetes Educ 2010;36:301–309

19. Tang TS, Funnell MM, Brown MB, Kurlander JE. Self-management support in "real-world" settings: an empowerment-based intervention. Patient Educ Couns 2010;79:178–184

20. Glazier RH, Bajcar J, Kennie NR, Willson K. A systematic review of interventions to improve diabetes care in socially disadvantaged populations. Diabetes Care 2006;29:1675–1688

21. Hawthorne K, Robles Y, Cannings-John R, Edwards AG. Culturally appropriate health education for type 2 diabetes mellitus in ethnic minority groups. Cochrane Database Syst Rev 2008;3:CD006424

22. Sarkisian CA, Brown AF, Norris KC, Wintz RL, Mangione CM. A systematic review of diabetes self-care interventions for older, African American, or Latino adults. Diabetes Educ 2003;29: 467–479

23. Chodosh J, Morton SC, Mojica W, et al. Meta-analysis: chronic disease self-management programs for older adults. Ann Intern Med 2005; 143:427–438

24. Peyrot M, Rubin RR. Behavioral and psychosocial interventions in diabetes: a conceptual review. Diabetes Care 2007;30:2433–2440

25. Naik AD, Palmer N, Petersen NJ, et al. Comparative effectiveness of goal setting in diabetes mellitus group clinics: randomized clinical trial. Arch Intern Med 2011;171:453–459

26. Duke SA, Colagiuri S, Colagiuri R. Individual patient education for people with type 2 diabetes mellitus. Cochrane Database Syst Rev 2009; 1:CD005268

27. Shah M, Kaselitz E, Heisler M. The role of community health workers in diabetes: update on current literature. Curr Diab Rep 2013;13: 163–171

28. Heisler M, Vijan S, Makki F, Piette JD. Diabetes control with reciprocal peer support versus nurse care management: a randomized trial. Ann Intern Med 2010;153:507–515

29. Long JA, Jahnle EC, Richardson DM, Loewenstein G, Volpp KG. Peer mentoring and financial incentives to improve glucose control in African American veterans: a randomized trial. Ann Intern Med 2012;156:416–424 30. Foster G, Taylor SJ, Eldridge SE, Ramsay J, Griffiths CJ. Self-management education programmes by lay leaders for people with chronic conditions. Cochrane Database Syst Rev 2007;4: CD005108

31. Duncan I, Birkmeyer C, Coughlin S, Li QE, Sherr D, Boren S. Assessing the value of diabetes education. Diabetes Educ 2009;35:752–760

32. Johnson TM, Murray MR, Huang Y. Associations between self-management education and comprehensive diabetes clinical care. Diabetes Spectr 2010;23:41–46

33. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach. Update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. Diabetes Care 2015; 38:140–149

34. Evert AB, Boucher JL, Cypress M, et al. Nutrition therapy recommendations for the management of adults with diabetes. Diabetes Care 2014;37(Suppl. 1):S120–S143

35. Kulkarni K, Castle G, Gregory R, et al.; Diabetes Care and Education Dietetic Practice Group. Nutrition practice guidelines for type 1 diabetes mellitus positively affect dietitian practices and patient outcomes. J Am Diet Assoc 1998;98:62–70

36. Rossi MCE, Nicolucci A, Di Bartolo P, et al. Diabetes Interactive Diary: a new telemedicine system enabling flexible diet and insulin therapy while improving quality of life: an open-label, international, multicenter, randomized study. Diabetes Care 2010;33:109–115

37. Scavone G, Manto A, Pitocco D, et al. Effect of carbohydrate counting and medical nutritional therapy on glycaemic control in type 1 diabetic subjects: a pilot study. Diabet Med 2010;27:477–479

38. UK Prospective Diabetes Study (UKPDS) Group. Effect of intensive blood-glucose control with metformin on complications in overweight patients with type 2 diabetes (UKPDS 34). Lancet 1998;352:854–865

39. Ziemer DC, Berkowitz KJ, Panayioto RM, et al. A simple meal plan emphasizing healthy food choices is as effective as an exchangebased meal plan for urban African Americans with type 2 diabetes. Diabetes Care 2003;26: 1719–1724

40. Wolf AM, Conaway MR, Crowther JQ, et al. Translating lifestyle intervention to practice in obese patients with type 2 diabetes: Improving Control with Activity and Nutrition (ICAN) study. Diabetes Care 2004;27:1570–1576

41. Coppell KJ, Kataoka M, Williams SM, Chisholm AW, Vorgers SM, Mann JI. Nutritional intervention in patients with type 2 diabetes who are hyperglycaemic despite optimised drug treatment—Lifestyle Over and Above Drugs in Diabetes (LOADD) study: randomised controlled trial. BMJ 2010;341:c3337

42. Tuomilehto J, Lindström J, Eriksson JG, et al.; Finnish Diabetes Prevention Study Group. Prevention of type 2 diabetes mellitus by changes in lifestyle among subjects with impaired glucose tolerance. N Engl J Med 2001; 344:1343–1350

43. Knowler WC, Barrett-Connor E, Fowler SE, et al.; Diabetes Prevention Program Research Group. Reduction in the incidence of type 2

diabetes with lifestyle intervention or metformin. N Engl J Med 2002;346:393-403

44. UK Prospective Diabetes Study 7. UK Prospective Diabetes Study 7: response of fasting plasma glucose to diet therapy in newly presenting type II diabetic patients, UKPDS Group. Metabolism 1990;39:905–912

45. Goldstein DJ. Beneficial health effects of modest weight loss. Int J Obes Relat Metab Disord 1992;16:397–415

46. Pastors JG, Warshaw H, Daly A, Franz M, Kulkarni K. The evidence for the effectiveness of medical nutrition therapy in diabetes management. Diabetes Care 2002;25:608–613

47. Sacks FM, Bray GA, Carey VJ, et al. Comparison of weight-loss diets with different compositions of fat, protein, and carbohydrates. N Engl J Med 2009;360:859–873

48. de Souza RJ, Bray GA, Carey VJ, et al. Effects of 4 weight-loss diets differing in fat, protein, and carbohydrate on fat mass, lean mass, visceral adipose tissue, and hepatic fat: results from the POUNDS LOST trial. Am J Clin Nutr 2012;95:614–625

49. Johnston BC, Kanters S, Bandayrel K, et al. Comparison of weight loss among named diet programs in overweight and obese adults: a meta-analysis. JAMA 2014;312:923–933

50. Jensen MD, Ryan DH, Apovian CM, et al.; American College of Cardiology/American Heart Association Task Force on Practice Guidelines; Obesity Society. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. J Am Coll Cardiol 2014;63(25 Pt B): 2985–3023

51. DAFNE Study Group. Training in flexible, intensive insulin management to enable dietary freedom in people with type 1 diabetes: Dose Adjustment For Normal Eating (DAFNE) randomised controlled trial. BMJ 2002;325:746

52. Delahanty LM, Nathan DM, Lachin JM, et al.; Diabetes Control and Complications Trial/Epidemiology of Diabetes. Association of diet with glycated hemoglobin during intensive treatment of type 1 diabetes in the Diabetes Control and Complications Trial. Am J Clin Nutr 2009;89:518–524

53. Wheeler ML, Dunbar SA, Jaacks LM, et al. Macronutrients, food groups, and eating patterns in the management of diabetes: a systematic review of the literature, 2010. Diabetes Care 2012;35:434–445

54. Thomas D, Elliott EJ. Low glycaemic index, or low glycaemic load, diets for diabetes mellitus. Cochrane Database Syst Rev 2009;1: CD006296

55. He M, van Dam RM, Rimm E, Hu FB, Qi L. Whole-grain, cereal fiber, bran, and germ intake and the risks of all-cause and cardiovascular disease-specific mortality among women with type 2 diabetes mellitus. Circulation 2010;121: 2162–2168

56. U.S. Department of Health and Human and Services, U.S. Department of Agriculture. Scientific Report of the 2015 Dietary Guidelines Advisory Committee [Internet], 2015. Available from http:// health.gov/dietaryguidelines/2015-scientificreport. Accessed 18 November 2015 57. Laurenzi A, Bolla AM, Panigoni G, et al. Effects of carbohydrate counting on glucose control and quality of life over 24 weeks in adult patients with type 1 diabetes on continuous subcutaneous insulin infusion: a randomized, prospective clinical trial (GIOCAR). Diabetes Care 2011;34:823–827

58. Sämann A, Mühlhauser I, Bender R, Kloos Ch, Müller UA. Glycaemic control and severe hypoglycaemia following training in flexible, intensive insulin therapy to enable dietary freedom in people with type 1 diabetes: a prospective implementation study. Diabetologia 2005; 48:1965–1970

59. Pan Y, Guo LL, Jin HM. Low-protein diet for diabetic nephropathy: a meta-analysis of randomized controlled trials. Am J Clin Nutr 2008; 88:660–666

60. Robertson L, Waugh N, Robertson A. Protein restriction for diabetic renal disease. Cochrane Database Syst Rev 2007;4:CD002181

61. Layman DK, Clifton P, Gannon MC, Krauss RM, Nuttall FQ. Protein in optimal health: heart disease and type 2 diabetes. Am J Clin Nutr 2008;87:1571S–1575S

62. Institute of Medicine. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids [Internet], 2002. Available from http://www.iom .edu/Reports/2002/Dietary-Reference-Intakesfor-Energy-Carbohydrate-Fiber-Fat-Fatty-Acids-Cholesterol-Protein-and-Amino-Acids.aspx. Accessed 1 October 2015

63. Estruch R, Ros E, Salas-Salvadó J, et al.; PREDIMED Study Investigators. Primary prevention of cardiovascular disease with a Mediterranean diet. N Engl J Med 2013;368:1279–1290

64. U.S. Department of Agriculture, U.S. Department of Health and Human and Services. Dietary guidelines for Americans [Internet], 2010. Available from http://health.gov/dietaryguidelines/2010. Accessed 1 October 2015

65. Ros E. Dietary cis-monounsaturated fatty acids and metabolic control in type 2 diabetes. Am J Clin Nutr 2003;78(Suppl.):6175–625S

66. Brehm BJ, Lattin BL, Summer SS, et al. Oneyear comparison of a high-monounsaturated fat diet with a high-carbohydrate diet in type 2 diabetes. Diabetes Care 2009;32:215–220

67. Shai I, Schwarzfuchs D, Henkin Y, et al.; Dietary Intervention Randomized Controlled Trial (DIRECT) Group. Weight loss with a low-carbohydrate, Mediterranean, or low-fat diet. N Engl J Med 2008;359:229–241

68. Brunerova L, Smejkalova V, Potockova J, Andel M. A comparison of the influence of a high-fat diet enriched in monounsaturated fatty acids and conventional diet on weight loss and metabolic parameters in obese non-diabetic and type 2 diabetic patients. Diabet Med 2007:24:533–540

69. Harris WS, Mozaffarian D, Rimm E, et al. Omega-6 fatty acids and risk for cardiovascular disease: a science advisory from the American Heart Association Nutrition Subcommittee of the Council on Nutrition, Physical Activity, and Metabolism; Council on Cardiovascular Nursing; and Council on Epidemiology and Prevention. Circulation 2009;119:902–907

70. Crochemore ICC, Souza AFP, de Souza ACF, Rosado EL. Omega-3 polyunsaturated fatty acid

supplementation does not influence body composition, insulin resistance, and lipemia in women with type 2 diabetes and obesity. Nutr Clin Pract 2012;27:553–560

71. Holman RR, Paul S, Farmer A, Tucker L, Stratton IM, Neil HA; Atorvastatin in Factorial with Omega-3 EE90 Risk Reduction in Diabetes Study Group. Atorvastatin in Factorial with Omega-3 EE90 Risk Reduction in Diabetes (AFORRD): a randomised controlled trial. Diabetologia 2009;52:50–59

72. Kromhout D, Geleijnse JM, de Goede J, et al. n-3 fatty acids, ventricular arrhythmia-related events, and fatal myocardial infarction in postmyocardial infarction patients with diabetes. Diabetes Care 2011;34:2515–2520

73. Bosch J, Gerstein HC, Dagenais GR, et al.; ORIGIN Trial Investigators. n-3 fatty acids and cardiovascular outcomes in patients with dysglycemia. N Engl J Med 2012;367:309–318

74. Bray GA, Vollmer WM, Sacks FM, Obarzanek E, Svetkey LP, Appel LJ; DASH Collaborative Research Group. A further subgroup analysis of the effects of the DASH diet and three dietary sodium levels on blood pressure: results of the DASH-Sodium Trial. Am J Cardiol 2004;94:222–227

75. Whelton PK, Appel LJ, Sacco RL, et al. Sodium, blood pressure, and cardiovascular disease: further evidence supporting the American Heart Association sodium reduction recommendations. Circulation 2012;126:2880–2889

76. Thomas MC, Moran J, Forsblom C, et al.; FinnDiane Study Group. The association between dietary sodium intake, ESRD, and allcause mortality in patients with type 1 diabetes. Diabetes Care 2011;34:861–866

77. Ekinci El, Clarke S, Thomas MC, et al. Dietary salt intake and mortality in patients with type 2 diabetes. Diabetes Care 2011;34:703–709

78. Maillot M, Drewnowski A. A conflict between nutritionally adequate diets and meeting the 2010 dietary guidelines for sodium. Am J Prev Med 2012;42:174–179

79. Pan XR, Li GW, Hu YH, et al. Effects of diet and exercise in preventing NIDDM in people with impaired glucose tolerance: the Da Qing IGT and Diabetes Study. Diabetes Care 1997; 20:537–544

80. Boulé NG, Haddad E, Kenny GP, Wells GA, Sigal RJ. Effects of exercise on glycemic control and body mass in type 2 diabetes mellitus: a meta-analysis of controlled clinical trials. JAMA 2001;286:1218–1227

81. Colberg SR, Riddell MC. Physical activity: regulation of glucose metabolism, clinicial management strategies, and weight control. In *American Diabetes Association/JDRF Type 1 Diabetes Sourcebook*. Alexandria, VA, American Diabetes Association, 2013, p. 249–292

82. Boulé NG, Kenny GP, Haddad E, Wells GA, Sigal RJ. Meta-analysis of the effect of structured exercise training on cardiorespiratory fitness in type 2 diabetes mellitus. Diabetologia 2003;46:1071–1081

83. Rejeski WJ, Ip EH, Bertoni AG, et al.; Look AHEAD Research Group. Lifestyle change and mobility in obese adults with type 2 diabetes. N Engl J Med 2012;366:1209–1217

84. Colberg SR, Sigal RJ, Fernhall B, et al.; American College of Sports Medicine; American Diabetes Association. Exercise and type 2 diabetes: the American College of Sports Medicine and the American Diabetes Association: joint position statement. Diabetes Care 2010;33: e147–e167

85. Janssen I, Leblanc AG. Systematic review of the health benefits of physical activity and fitness in school-aged children and youth. Int J Behav Nutr Phys Act 2010;7:40

86. U.S. Department of Health and Human Services. 2008 physical activity guidelines for Americans [Internet], 2008. Available from http://www.health.gov/paguidelines/ guidelines/default.aspx. Accessed 1 October 2015

87. Katzmarzyk PT, Church TS, Craig CL, Bouchard C. Sitting time and mortality from all causes, cardiovascular disease, and cancer. Med Sci Sports Exerc 2009;41:998–1005

88. Sigal RJ, Kenny GP, Wasserman DH, Castaneda-Sceppa C. Physical activity/exercise and type 2 diabetes. Diabetes Care 2004;27:2518–2539

89. Church TS, Blair SN, Cocreham S, et al. Effects of aerobic and resistance training on hemoglobin A1c levels in patients with type 2 diabetes: a randomized controlled trial. JAMA 2010;304:2253–2262

90. Bax JJ, Young LH, Frye RL, Bonow RO, Steinberg HO, Barrett EJ; American Diabetes Association. Screening for coronary artery disease in patients with diabetes. Diabetes Care 2007; 30:2729–2736

91. American Diabetes Association, JDRF. American Diabetes Association/JDRF Type 1 Diabetes Sourcebook. Peters A, Laffel L, Eds. Alexandria, VA, American Diabetes Association, 2013

92. Colberg SR. Exercise and Diabetes: A Clinician's Guide to Prescribing Physical Activity. Alexandria, VA, American Diabetes Association, 2013

93. Lemaster JW, Reiber GE, Smith DG, Heagerty PJ, Wallace C. Daily weight-bearing activity does not increase the risk of diabetic foot ulcers. Med Sci Sports Exerc 2003;35: 1093–1099

94. Smith AG, Russell J, Feldman EL, et al. Lifestyle intervention for pre-diabetic neuropathy. Diabetes Care 2006;29:1294–1299

95. Spallone V, Ziegler D, Freeman R, et al.; Toronto Consensus Panel on Diabetic Neuropathy. Cardiovascular autonomic neuropathy in diabetes: clinical impact, assessment, diagnosis, and management. Diabetes Metab Res Rev 2011;27: 639–653

96. Pop-Busui R, Evans GW, Gerstein HC, et al.; Action to Control Cardiovascular Risk in Diabetes Study Group. Effects of cardiac autonomic dysfunction on mortality risk in the Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial. Diabetes Care 2010;33:1578–1584

97. Suarez L, Barrett-Connor E. Interaction between cigarette smoking and diabetes mellitus in the prediction of death attributed to cardiovascular disease. Am J Epidemiol 1984;120:670– 675

98. Jankowich M, Choudhary G, Taveira TH, Wu WC. Age-, race-, and gender-specific prevalence of diabetes among smokers. Diabetes Res Clin Pract 2011;93:e101–e105

99. Voulgari C, Katsilambros N, Tentolouris N. Smoking cessation predicts amelioration of microalbuminuria in newly diagnosed type 2 diabetes mellitus: a 1-year prospective study. Metabolism 2011;60:1456–1464

100. Ranney L, Melvin C, Lux L, McClain E, Lohr KN. Systematic review: smoking cessation intervention strategies for adults and adults in special populations. Ann Intern Med 2006;145: 845–856

101. Clair C, Rigotti NA, Porneala B, et al. Association of smoking cessation and weight change with cardiovascular disease among adults with and without diabetes. JAMA 2013;309:1014–1021

102. Schraufnagel DE, Blasi F, Drummond MB, et al.; Forum of International Respiratory Societies. Electronic cigarettes. A position statement of the Forum of International Respiratory Societies. Am J Respir Crit Care Med 2014;190:611– 618

103. Bam TS, Bellew W, Berezhnova I, et al.; Tobacco Control Department International Union Against Tuberculosis and Lung Disease. Position statement on electronic cigarettes or electronic nicotine delivery systems. Int J Tuberc Lung Dis 2014;18:5–7

104. Bhatnagar A, Whitsel LP, Ribisl KM, et al.; American Heart Association Advocacy Coordinating Committee, Council on Cardiovascular and Stroke Nursing, Council on Clinical Cardiology, and Council on Quality of Care and Outcomes Research. Electronic cigarettes: a policy statement from the American Heart Association. Circulation 2014;130:1418–1436

105. Strikas RA; Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices (ACIP); ACIP Child/Adolescent Immunization Work Group. Advisory Committee on Immunization Practices recommended immunization schedules for persons aged 0 through 18 years—United States, 2015. MMWR Morb Mortal Wkly Rep 2015;64:93-94 106. Kim DK, Bridges CB, Harriman KH; Centers for Disease Control and Prevention (CDC); Advisory Committee on Immunization Practices (ACIP); ACIP Adult Immunization Work Group. Advisory Committee on Immunization Practices recommended immunization schedule for adults aged 19 years or older—United States. 2015. MMWR Morb Mortal Wkly Rep 2015;64: 91-92

107. Valdez R, Narayan KM, Geiss LS, Engelgau MM. Impact of diabetes mellitus on mortality associated with pneumonia and influenza among non-Hispanic black and white US adults. Am J Public Health 1999;89:1715–1721

108. Colquhoun AJ, Nicholson KG, Botha JL, Raymond NT. Effectiveness of influenza vaccine in reducing hospital admissions in people with diabetes. Epidemiol Infect 1997;119:335–341 109. Smith SA, Poland GA. Use of influenza and pneumococcal vaccines in people with diabetes.

Diabetes Care 2000;23:95–108 110. Anderson RJ, Grigsby AB, Freedland KE, et al. Anxiety and poor glycemic control: a meta-analytic review of the literature. Int J Psychiatry Med 2002;32:235–247

111. Delahanty LM, Grant RW, Wittenberg E, et al. Association of diabetes-related emotional distress with diabetes treatment in primary care

patients with type 2 diabetes. Diabet Med 2007; 24:48–54

112. Anderson RJ, Freedland KE, Clouse RE, Lustman PJ. The prevalence of comorbid depression in adults with diabetes: a meta-analysis. Diabetes Care 2001;24:1069–1078

113. Kovacs Burns K, Nicolucci A, Holt RIG, et al.; DAWN2 Study Group. Diabetes Attitudes, Wishes and Needs second study (DAWN2): cross-national benchmarking indicators for family members living with people with diabetes. Diabet Med 2013;30:778–788

114. Harkness E, Macdonald W, Valderas J, Coventry P, Gask L, Bower P. Identifying psychosocial interventions that improve both physical and mental health in patients with diabetes: a systematic review and meta-analysis. Diabetes Care 2010;33:926–930

115. Bot M, Pouwer F, Zuidersma M, van Melle JP, de Jonge P. Association of coexisting diabetes and depression with mortality after myocardial infarction. Diabetes Care 2012;35:503–509 116. Scherrer JF, Garfield LD, Chrusciel T, et al. Increased risk of myocardial infarction in depressed patients with type 2 diabetes. Diabetes Care 2011;34:1729–1734

117. Chen PC, Chan YT, Chen HF, Ko MC, Li CY. Population-based cohort analyses of the bidirectional relationship between type 2 diabetes and depression. Diabetes Care 2013;36:376– 382

118. Pan A, Keum N, Okereke OI, et al. Bidirectional association between depression and metabolic syndrome: a systematic review and meta-analysis of epidemiological studies. Diabetes Care 2012;35:1171–1180

119. Nicolucci A, Kovacs Burns K, Holt RIG, et al.; DAWN2 Study Group. Diabetes Attitudes, Wishes and Needs second study (DAWN2): cross-national benchmarking of diabetes-related psychosocial outcomes for people with diabetes. Diabet Med 2013;30:767–777

120. Fisher L, Hessler DM, Polonsky WH, Mullan J. When is diabetes distress clinically meaningful? Establishing cut points for the Diabetes Distress Scale. Diabetes Care 2012;35: 259–264

121. Fisher L, Glasgow RE, Strycker LA. The relationship between diabetes distress and clinical depression with glycemic control among patients with type 2 diabetes. Diabetes Care 2010;33:1034–1036

122. Aikens JE. Prospective associations between emotional distress and poor outcomes in type 2 diabetes. Diabetes Care 2012;35:2472– 2478

123. Fisher L, Glasgow RE, Mullan JT, Skaff MM, Polonsky WH. Development of a brief diabetes distress screening instrument. Ann Fam Med 2008;6:246–252

124. McGuire BE, Morrison TG, Hermanns N, et al. Short-form measures of diabetes-related emotional distress: the Problem Areas in Diabetes Scale (PAID)-5 and PAID-1. Diabetologia 2010;53:66–69

125. Gary TL, Safford MM, Gerzoff RB, et al. Perception of neighborhood problems, health behaviors, and diabetes outcomes among adults with diabetes in managed care: the Translating Research Into Action for Diabetes (TRIAD) study. Diabetes Care 2008;31:273–278 126. Zhang X, Norris SL, Gregg EW, Cheng YJ, Beckles G, Kahn HS. Depressive symptoms and mortality among persons with and without diabetes. Am J Epidemiol 2005;161:652–660

127. Rubin RR, Peyrot M. Psychological issues and treatments for people with diabetes. J Clin Psychol 2001;57:457–478

128. Young-Hyman DL, Davis CL. Disordered eating behavior in individuals with diabetes: importance of context, evaluation, and classification. Diabetes Care 2010;33:683–689

129. Beverly EA, Hultgren BA, Brooks KM, Ritholz MD, Abrahamson MJ, Weinger K. Understanding physicians' challenges when treating type 2 diabetic patients' social and emotional difficulties: a qualitative study. Diabetes Care 2011;34:1086–1088

130. Ciechanowski P. Diapression: an integrated model for understanding the experience of individuals with co-occurring diabetes and depression. Clin Diabetes 2011;29:43–49

131. Katon WJ, Lin EH, Von Korff M, et al. Collaborative care for patients with depression and chronic illnesses. N Engl J Med 2010;363:2611– 2620

132. Selvin E, Coresh J, Brancati FL. The burden and treatment of diabetes in elderly individuals in the U.S. Diabetes Care 2006;29:2415–2419

133. Grant RW, Ashburner JM, Hong CS, Chang Y, Barry MJ, Atlas SJ. Defining patient complexity from the primary care physician's perspective: a cohort study. Ann Intern Med 2011;155: 797–804

134. Tinetti ME, Fried TR, Boyd CM. Designing health care for the most common chronic condition—multimorbidity. JAMA 2012;307: 2493–2494

135. Sudore RL, Karter AJ, Huang ES, et al. Symptom burden of adults with type 2 diabetes across the disease course: Diabetes & Aging Study. J Gen Intern Med 2012;27:1674–1681

136. Borgnakke WS, Ylöstalo PV, Taylor GW, Genco RJ. Effect of periodontal disease on diabetes: systematic review of epidemiologic observational evidence. J Periodontol 2013;84 (Suppl.):S135–S152

137. El-Serag HB, Tran T, Everhart JE. Diabetes increases the risk of chronic liver disease and

hepatocellular carcinoma. Gastroenterology 2004;126:460-468

138. American Gastroenterological Association. American Gastroenterological Association medical position statement: nonalcoholic fatty liver disease. Gastroenterology 2002;123:1702– 1704

139. Li C, Ford ES, Zhao G, Croft JB, Balluz LS, Mokdad AH. Prevalence of self-reported clinically diagnosed sleep apnea according to obesity status in men and women: National Health and Nutrition Examination Survey, 2005-2006. Prev Med 2010:51:18–23

140. West SD, Nicoll DJ, Stradling JR. Prevalence of obstructive sleep apnoea in men with type 2 diabetes. Thorax 2006;61:945–950

141. Foster GD, Sanders MH, Millman R, et al.; Sleep AHEAD Research Group. Obstructive sleep apnea among obese patients with type 2 diabetes. Diabetes Care 2009;32:1017–1019

142. Shaw JE, Punjabi NM, Wilding JP, Alberti KG, Zimmet PZ; International Diabetes Federation Taskforce on Epidemiology and Prevention. Sleep-disordered breathing and type 2 diabetes: a report from the International Diabetes Federation Taskforce on Epidemiology and Prevention. Diabetes Res Clin Pract 2008;81:2–12

143. Suh S, Kim K-W. Diabetes and cancer: is diabetes causally related to cancer? Diabetes Metab J 2011;35:193–198

144. Giovannucci E, Harlan DM, Archer MC, et al. Diabetes and cancer: a consensus report. Diabetes Care 2010:33:1674–1685

145. Janghorbani M, Van Dam RM, Willett WC, Hu FB. Systematic review of type 1 and type 2 diabetes mellitus and risk of fracture. Am J Epidemiol 2007;166:495–505

146. Vestergaard P. Discrepancies in bone mineral density and fracture risk in patients with type 1 and type 2 diabetes—a meta-analysis. Osteoporos Int 2007;18:427–444

147. Schwartz AV, Vittinghoff E, Bauer DC, et al.; Study of Osteoporotic Fractures (SOF) Research Group; Osteoporotic Fractures in Men (MrOS) Research Group; Health, Aging, and Body Composition (Health ABC) Research Group. Association of BMD and FRAX score with risk of fracture in older adults with type 2 diabetes. JAMA 2011;305:2184–2192

148. Kahn SE, Zinman B, Lachin JM, et al.; Diabetes Outcome Progression Trial (ADOPT) Study Group. Rosiglitazone-associated fractures in type 2 diabetes: an Analysis from A Diabetes Outcome Progression Trial (ADOPT). Diabetes Care 2008;31:845–851

149. Taylor SI, Blau JE, Rother KI. Possible adverse effects of SGLT2 inhibitors on bone. Lancet Diabetes Endocrinol 2015;3:8–10

150. Dhindsa S, Miller MG, McWhirter CL, et al. Testosterone concentrations in diabetic and nondiabetic obese men. Diabetes Care 2010; 33:1186–1192

151. Bhasin S, Cunningham GR, Hayes FJ, et al.; Endocrine Society Task Force. Testosterone therapy in men with androgen deficiency syndromes: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab 2010;95: 2536–2559

152. Khader YS, Dauod AS, El-Qaderi SS, Alkafajei A, Batayha WQ. Periodontal status of diabetics compared with nondiabetics: a meta-analysis. J Diabetes Complications 2006;20:59–68

153. Bainbridge KE, Hoffman HJ, Cowie CC. Diabetes and hearing impairment in the United States: audiometric evidence from the National Health and Nutrition Examination Survey, 1999 to 2004. Ann Intern Med 2008;149:1–10

154. Cukierman T, Gerstein HC, Williamson JD. Cognitive decline and dementia in diabetes systematic overview of prospective observational studies. Diabetologia 2005;48:2460–2469

155. Biessels GJ, Staekenborg S, Brunner E, Brayne C, Scheltens P. Risk of dementia in diabetes mellitus: a systematic review. Lancet Neurol 2006;5:64–74

156. Ohara T, Doi Y, Ninomiya T, et al. Glucose tolerance status and risk of dementia in the community: the Hisayama study. Neurology 2011;77:1126–1134

157. Launer LJ, Miller ME, Williamson JD, et al.; ACCORD MIND Investigators. Effects of intensive glucose lowering on brain structure and function in people with type 2 diabetes (ACCORD MIND): a randomised open-label substudy. Lancet Neurol 2011;10:969–977