

With respect to other meal patterns, there are limited RCT data available that address prevention of CMD outcomes in persons with prediabetes or metabolic syndrome. The DASH diet has been shown to reduce BP and is particularly effective in individuals who were hypertensive at baseline and/or self-identified as African American.^{817,818} Adherence to a DASH diet is also associated with a low prevalence of DM.^{819–821} Low-fat meal plans in the context of a comprehensive lifestyle intervention have been shown to promote weight loss, improve glucose tolerance, and prevent DM in large RCTs enrolling persons with obesity and IGT.^{811,822–828} A large number of cohort studies and epidemiological data demonstrate that vegetarian and vegan diets confer metabolic benefits and are associated with a lower risk of developing T2D.^{820,829–833} In a meta-analysis of 11 cohort studies,⁷¹⁵ a low-carbohydrate diet was no different than a high-carbohydrate diet regarding incidence of DM^{715,834} and could be harmful if fat sources are derived from red meat.⁸³⁵ Given the limited evidence, it is unclear which meal pattern is optimal. There is a large body of data indicating that isocaloric substitution of specific macronutrients can improve insulin sensitivity assessed by clamp studies and CVD risk factors.⁸³⁶ These data would generally support macronutrient intake as follows: (1) limitations on fat intake, (2) emphasis on poly/mono-unsaturated fats over saturated fats, (3) no trans fats,⁸³⁵ (4) complex over simple carbohydrates, (5) whole grains over refined grains⁹³⁴, (6) fruits and vegetables,⁸³⁷ (7) dietary fiber,⁸³⁸ and (8) reduced consumption of processed food.⁸³⁹ Dietary enrichment of these macronutrients can enhance insulin sensitivity,⁸³⁶ aligning with the Mediterranean diet and other meal patterns that are epidemiologically associated with reduced prevalence of T2D,⁸³⁹ and predictably would be beneficial based on the role of insulin resistance in the pathophysiology of CMD. Indeed, these foods and macronutrients coincide with favorable scores on the Healthy Eating Index-2010 (HEI-2010), the Alternative HEI-2010 (AHEI-2010), the Alternative Mediterranean Diet Score, and the DASH scores, which are associated epidemiologically with lower prevalence of DM.^{723,840}

There is a plethora of evidence in persons with prediabetes and metabolic syndrome that regular exercise can lower glycemia, improve CVD risk factors, and prevent or delay progression to DM, either in the form of an exercise program per se or as part of a comprehensive lifestyle plan.^{841–851} As is the case for persons with T2D, studies have demonstrated beneficial effects of both aerobic and resistance exercise and additive benefits when both forms of exercise are combined.^{727,847–852} The physical activity program optimally includes aerobic exercise, which should begin at a low level to allow a person to increase the intensity and duration of the exercise over time. Various guidelines have recommended that, ideally, a person should achieve at least 150 minutes per week of moderately intense aerobic exercise accomplished in 3 to 5 sessions.^{674,852,853} High-intensity interval training can be used to achieve comparable metabolic benefits of moderate aerobic exercise with less of a time commitment.⁸⁵⁴ A resistance exercise program should be added and should consist of single-set repetitions targeting the major muscle groups 2 to 3 times per week.^{674,852,853} Despite these recommendations, less intense exercise and walking programs can reduce risk of DM.^{846,855} A final component of a physical activity program is to reduce sedentary behavior and increase active leisure activity.^{856–859} The physical activity prescription should be compatible with individual preferences and take into account any health-related or physical limitations.⁶⁷⁴

In persons with ABCD (both overweight or with obesity) and prediabetes and/or metabolic syndrome, weight loss is a highly effective way to prevent progression to T2D.⁶⁷⁴ In addition, weight reduction prevents or treats multiple CVD risk factors and additional complications of ABCD.⁶⁷⁴ Whether due to lifestyle therapy, obesity medications, or bariatric surgery, weight loss has been

shown to (1) enhance insulin sensitivity; (2) prevent or delay progression to T2D particularly in high-risk persons with prediabetes or metabolic syndrome; (3) improve hepatic steatosis; (4) lower BP; (5) improve dyslipidemia; and (6) ameliorate biomarkers of CVD risk, including CRP, interleukin 6 and other markers of inflammation, fibrinogen levels, and serum adiponectin concentrations.⁶⁷⁴ Thus, weight loss is perhaps the most effective therapeutic approach for preventing the progression of CMD to T2D and/or CVD events.

In persons with ABCD, the principles of lifestyle therapy are the same as those that generally apply in prediabetes and metabolic syndrome except that the meal plan is presented in a reduced-calorie format to achieve weight loss. Any one of the reviewed meal plans (Mediterranean, low-fat, low-carbohydrate, vegetarian, vegan, and DASH diets) can be used as diets that feature a healthy composition of foods and macronutrients that promote insulin sensitivity⁸³⁶ and are associated with improvements in CMD outcomes as defined by the HEI^{723,840} and other epidemiological data. Although any of these healthy eating patterns can safely be used in the short term for weight reduction and improvements in CVD risk factors, only the Mediterranean diet has been shown to be cardioprotective in the long term. To accomplish weight loss, the incorporation of very low-calorie diets and meal substitutes into an overall dietary plan has been shown to be effective in achieving greater degrees of weight loss.^{689,860}

Regarding lifestyle interventions in persons who have ABCD and prediabetes, 3 major RCTs, the Diabetes Prevention Program, the Finnish Diabetes Study, and the Da Qing Study, all demonstrated that lifestyle/behavioral therapy featuring a reduced-calorie diet (eg, caloric deficits of 500 to 1000 calories/day) and physical activity are highly effective in preventing T2D.^{811,822–828} These lifestyle interventions also improved other aspects of CMD including improvements in insulin sensitivity and CVD risk factors, such as BP, lipids, and markers of inflammation. In addition, long-term follow-up of participants in the Da Qing Study revealed that CVD events and mortality were reduced when comparing the combined subgroups treated with diet and exercise with the controls.⁸²⁸ The Diabetes Prevention Program study randomized persons with IGT to ordinary care, metformin, and lifestyle intervention subgroups, and after 4 years, lifestyle modification reduced progression to T2D by 58% and metformin by 31%, compared with placebo.⁸¹¹ Participants achieved approximately 6% mean weight loss at 2 years and 4% weight loss at 4 years in the lifestyle intervention arm, and there was a progressive 16% reduction in T2D risk with every kilogram of weight loss.⁸²² With observational follow-up after termination of the study, there was still a significant reduction in the cumulative incidence of T2D in the lifestyle treatment group at 10 years, despite the fact that BMI levels had equalized among the 3 treatment arms.^{823,824} The Diabetes Prevention Program was a resource-intensive efficacy trial and was not designed to be directly deliverable in real-world settings. The translation of the structured lifestyle intervention used in the Diabetes Prevention Program to community-based programs, commercial programs, and programs using remote technologies have achieved less weight loss than observed in the Diabetes Prevention Program trial itself.^{861–869} Despite limited weight loss, some efforts have produced modest improvements in metabolic parameters and, when measured, reductions in incidence of DM. A meta-analysis of 44 Diabetes Prevention Program translation studies reported an average 9.3-month weight loss of 3.77 kg from participants' baseline weight and a decrease in fasting glucose of 2.4 mg/dL.⁸⁶⁵ Another meta-analysis of 63 real-world DM prevention efforts demonstrated a weight loss of 2.2 kg in participants and 0.8 kg in controls, but still led to a reduction in incident DM by 25%.⁸⁶⁶ Since the degree of DM prevention is proportional to the degree of weight loss,⁸²² these efforts at translation would predictably be less effective regarding prevention of DM.