

Targeting diabetes: The benefits of an integrative approach

As patients with type 2 diabetes become increasingly interested in alternative therapies, you need to know what to recommend—or advise against. This evidence-based review and at-a-glance table will help.

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PRACTICE RECOMMENDATIONS

➤ *Tell patients with type 2 diabetes mellitus (T2DM) that chromium and fiber appear to have a beneficial effect on glycemic control, while the benefits of other dietary supplements are not known. (C)*

➤ *Recommend acupuncture for patients with T2DM and peripheral neuropathy, bladder dysfunction, or symptoms of other comorbidities that have not fully responded to conventional therapy. (B)*

➤ *Advise patients that biofeedback and meditation are more likely than other types of stress reduction to improve glycemic control. (C)*

Strength of recommendation (SOR)

- (A)** Good-quality patient-oriented evidence
- (B)** Inconsistent or limited-quality patient-oriented evidence
- (C)** Consensus, usual practice, opinion, disease-oriented evidence, case series

Integrative medicine—an approach that combines conventional and alternative therapies with an emphasis on natural, less invasive evidence-based options—is well suited to the management of complex chronic diseases like type 2 diabetes mellitus (T2DM). And we've found that patients with T2DM are increasingly interested in integrative strategies, most of which involve self-management and lifestyle changes. They're often motivated by the desire to limit the number of medications they're taking or to avoid diabetes drugs entirely. In many cases, patients also hope to alleviate symptoms of comorbidities that have not fully responded to conventional treatment, such as peripheral neuropathy, bladder dysfunction, and gastroparesis.

As a family physician, you're likely to be asked about unconventional approaches to diabetes and to be in a position to recommend alternative therapies in conjunction with pharmaceutical management of T2DM. In both cases, you need to know which integrative strategies have evidence to support their use. We created the text and tables that follow with this in mind.

Nutrition and weight loss: What works?

To reduce cardiovascular disease risk factors, patients with T2DM are advised to eliminate trans fats and to limit saturated fat to <7% of total caloric intake. A moderate weight loss (5% of body weight) has been found to improve insulin action, decrease fasting blood glucose (FBG) concentrations, and reduce the need for diabetes medications.^{1,2} One small retrospective cohort study (N=72) found that a 10% weight loss was associated with a reduction in glycosylated hemoglobin (HbA1c) of 0.81 percentage points.³ Weight maintenance is also an important element of diabetes management, even for patients who have not been able to lose their excess weight.²

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TABLE 1

3 diets for type 2 diabetes: Which is best for your patient?

Type of diet	Description	Effectiveness
Low glycemic index (GI)*	Emphasizes carbohydrates and other foods with a low GI, which result in a more gradual rise in glucose and insulin release	Reduction of 0.4-0.5 in HbA1c ⁴
Mediterranean [†]	Eliminates proinflammatory fats and restores healthy omega 3/omega 6 fatty acid balance; high in fruits and vegetables, unsaturated fats, fish, and grains with a low GI index and moderate alcohol/red wine consumption	Reduction of 0.1-0.6 in HbA1c ¹⁵
Vegetarian	Focuses on fruits and vegetables and foods low in saturated fat; tends to be higher in fiber and lower in calories than other diets	Reduction of 1.23 in HbA1c ^{†6} ; promotes weight loss

*A list of the glycemic index per serving of dozens of common foods is available at http://www.health.harvard.edu/newsweek/Glycemic_index_and_glycemic_load_for_100_foods.htm.

[†]A Mediterranean diet has also been shown to reduce the risk of diabetes by 83%.⁵

[†]Based on one RCT.

GI, glycemic index; HbA1c, glycosylated hemoglobin; T2DM, type 2 diabetes mellitus.

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The effectiveness of the Mediterranean diet—despite its higher carbohydrate content—suggests that treating systemic inflammation may help to reduce insulin resistance and hyperglycemia.

American Diabetes Association (ADA) guidelines do not endorse a specific diet. But patients often ask for dietary advice and want to know how specific diet plans and food choices will affect glycemic control and comorbid conditions. You can present the evidence (TABLE 1)⁴⁻⁶ of the effectiveness of a low glycemic index (GI) diet, a Mediterranean diet, and a vegetarian diet and point out that the best diet for a particular patient is the one best suited to his or her lifestyle and dietary goals.

■ **Low glycemic index diet.** The 2013 ADA guidelines acknowledge that a dietary regimen with a low glycemic index (GI) may be more beneficial for glycemic control than a diet based on total carbohydrate count alone.⁷

A Cochrane review of 11 small studies found a reduction in HbA1c of 0.5 (95% confidence interval [CI], -0.9 to -0.1; *P*=.02) in patients with T2DM who followed a low GI diet for 4 weeks or more. Patients on this diet also had a significant reduction in hypoglycemic events compared with those on other dietary regimens;⁴ one of the studies included in the meta-analysis also found a statistically significant increase in high-density lipoprotein cholesterol (HDL-C) in those on the low GI diet.⁸

■ **Mediterranean diet.** Rich in fruits and vegetables and unsaturated fats, fish, and grains with a low GI, the Mediterranean diet has a higher carbohydrate and fat content than a portion-controlled diet formerly recommended by the ADA. (As noted earlier, current ADA guidelines do not recommend a particular diet).

A systematic review of 5 randomized controlled trials (RCTs) (N=1077) found improved glycemic control in patients on a Mediterranean diet compared with those on other commonly used diets, such as low fat and portion-controlled regimens. Fasting blood glucose (FBG) fell between 7 and 40 mg/dL and HbA1c by 0.1 to 0.6 in studies that ranged from 6 months to 2 years.⁵ The effectiveness of the Mediterranean diet, despite its higher carbohydrate content, suggests that treating systemic inflammation may help to reduce insulin resistance and hyperglycemia.

■ **Vegetarian diet.** Vegetarian and vegan diets also offer potential benefits in the management of T2DM—including the fact that they tend to be lower in calories than other dietary regimens and therefore more likely to promote weight loss. In one 22-week RCT (N=99), those who were ran-

domized to a low-fat vegan diet lost more weight (6.5 vs 3.1 kg; $P < .001$) and had a larger decrease in HbA1c (-1.23 vs -0.38; $P < .01$) and low density lipoprotein cholesterol (LDL-C) (-22.6 vs -10.7 mg/dL; $P = .02$) compared with those following a portion-controlled ADA diet. Glycemic change correlated with the change in body weight.⁶

Choose carefully among the supplements

Metformin was derived from *Galega officinalis*—a plant (sometimes called goat's rue, or French lilac) used by Europeans as a traditional treatment for diabetes since the Middle Ages.⁹ More than 400 dietary supplements have been reported to have beneficial effects for patients with diabetes, including plant-based products such as fenugreek, prickly pear, and ginseng; vitamins, and minerals. But in most cases, the evidence is of poor quality (TABLE 2). Only one—cinnamon—has Level I evidence (ie, evidence derived from at least one well-designed RCT).

Two recent meta-analyses of cinnamon supplementation for patients with diabetes—one from 2012 and the other from 2011—yielded different results. The 2012 evidence comes from a Cochrane review showing that 3 types of cinnamon—true cinnamon (*Cinnamomum zeylanicum*), Chinese cinnamon (*C cassia*), and Indonesian cinnamon (*C burmanni*)—had no effect on HbA1c in patients with type 1 or T2DM and a borderline effect on FBG.¹⁰ However, the 2011 meta-analysis found that cinnamon supplementation led to a significant improvement in FBG.¹¹

The bottom line? The evidence is inconclusive.

Fiber and chromium stand out

Fiber. Whether taken as a supplement or in foods such as chickpeas, beans, peas, and lentils, fiber has been shown to improve glycemic control.^{12,13} The ADA recommends 25 to 35 g of dietary fiber daily.¹³

■ **Chromium,** a trace mineral thought to be a necessary cofactor for insulin regulation and glucose metabolism, is present in many foods, especially brewer's yeast, liver, carrots, potatoes, broccoli, and spinach. Nota-

bly, however, refining grains and processing foods removes most absorbable chromium. Patients with T2DM may therefore benefit from chromium supplementation: A 2007 systematic review found that it lowered their HbA1c by an average of 0.6.¹⁴

What about other supplements?

The ADA does not generally support the use of micronutrient supplements for patients with diabetes, but notes that individuals at increased risk for deficiencies (eg, those following very-low-calorie diets, the elderly, and strict vegetarians) may benefit from multivitamin supplements.

■ **Magnesium.** Dietary sources of magnesium, which is involved in insulin secretion, binding, and activity, include whole grains, leafy green vegetables, legumes, and nuts. A deficiency is associated with decreased absorption (in patients with diets high in processed food, for example) or increased elimination (in those who ingest large quantities of alcohol or caffeine or take diuretics or birth control pills). A 2006 meta-analysis found that magnesium supplements led to an improvement in FBG, but did not significantly lower HbA1c in patients with T2DM.¹⁵

■ **Vitamin D.** Although individuals with the highest vitamin D levels (>25 ng/mL) have a 43% lower risk of *developing* diabetes,¹⁶ it is not known whether vitamin D supplements are beneficial to patients with T2DM. (For more on vitamin D supplementation, see the Practice Alert on page 368.)

■ **Vitamin E.** A fat-soluble antioxidant found in vegetable oil, nuts, and green leafy vegetables, vitamin E's best-studied component is alpha-tocopherol. A 2011 meta-analysis found vitamin E supplementation to have a beneficial effect in patients with T2DM—but only for the subset of patients who had both low serum vitamin E levels and an HbA1c >8.0%.¹⁷ Observational studies have raised questions about the safety of vitamin E supplements, and a 2005 meta-analysis concluded that high-dose vitamin E supplementation (≥ 400 IU/d) may increase all-cause mortality.¹⁸

What about omega-3 PUFAs?

The role of omega-3 polyunsaturated fatty acids (PUFAs) in the prevention and treat-



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TABLE 2

Which alternative therapies will benefit patients with type 2 diabetes? An at-a-glance summary

Therapy	Evidence of efficacy
Dietary	
Low GI diet ⁴	HbA1c reduction of 0.4-0.5
Mediterranean diet ⁵	HbA1c reduction of 0.1-0.6; reduces the risk of diabetes by 83%
Vegetarian diet ⁶	HbA1c reduction of 1.23;* most likely to result in weight loss
Weight loss ³	10% weight loss associated with reduction of 0.81 in HbA1c*
Supplementation	
ALA ^{19,20}	Inconclusive
Chromium ¹⁴	HbA1c reduction of 0.6
Cinnamon ^{10,11}	Inconclusive
Fiber ^{12,13}	HbA1c reduction of 0.26
Magnesium ¹⁵	HbA1c reduction of 0.31
Omega-3 PUFAs	No effect on glycemic control
Vitamin D ¹⁶	Not known
Vitamin E ¹⁷	HbA1c reduction of 0.58 (in patients with baseline HbA1c >8.0% and vitamin E deficiency)
Physical activity²¹	
Exercise duration >150 min/wk ≤150 min/wk	HbA1c reduction of 0.89 HbA1c reduction of 0.36
Exercise, structured -Aerobic alone -Resistance alone	HbA1c reduction of 0.73 HbA1c reduction of 0.57
Physical activity advice + dietary advice	HbA1c reduction of 0.58
Mind-body	
Biofeedback ²³	HbA1c reduction of 0.6*
Meditation ³¹	HbA1c reduction of 0.5*
Qigong/Tai Chi ³³⁻³⁵	Inconclusive
Yoga ²⁵⁻²⁷	Inconclusive
Manual medicine	
Acupuncture ³⁶⁻⁴⁰	Inconclusive for glycemic control; statistically significant symptom improvement for peripheral neuropathy and bladder dysfunction
Chiropractic	Not studied
Massage/energy therapy ⁴²⁻⁴⁵	Inconclusive
Reflexology ^{46,47}	Inconclusive for glycemic control; improvement in PAD*

*Based on one RCT.

ALA, alpha-lipoic acid; GI, glycemic index; HbA1c, glycosylated hemoglobin; PAD, peripheral arterial disease; PUFA, polyunsaturated fatty acid; RCT, randomized controlled trial.

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For patients with type 2 diabetes, higher intensity activity does not appear to lead to greater improvement in glycemic control compared with moderate intensity activity.

ment of diseases related to inflammation has garnered much attention for years. But there is no evidence that taking omega-3 PUFAs lowers the risk of macrovascular outcomes or mortality for patients with T2DM.

■ **Alpha lipoic acid (ALA)**, an anti-oxidant made by the body and found in very small amounts in foods, is widely used in Europe, and has shown promise in the treatment of diabetic neuropathy. Small studies have found that ALA may reduce oxidative stress and improve insulin sensitivity in patients with diabetes,¹⁹ and a recent small RCT showed a statistically significant decrease in FBG and postprandial glucose after 8 weeks of taking it.²⁰

How to get patients moving

The ADA recommends that patients with T2DM get 150 minutes per week of moderate intensity aerobic activity (at 50%-70% of maximum heart rate), spread over at least 3 days a week and with no more than 2 consecutive days without activity. Resistance training provides additional benefit; the ADA recommends that patients engage in resistance training at least twice a week, using 5 major muscle groups.⁷ Regular exercise helps both weight reduction and glucose uptake, but simply pointing that out to patients with T2DM is not enough.

■ **What works?** A large meta-analysis found that structured exercise training (in most studies, this consisted of 2-5 supervised sessions weekly for 12-16 weeks) led to a decrease in HbA1c (-0.67; 95% CI, -0.84 to -0.49). When the structured exercise was aerobic, HbA1c declined by 0.73 (95% CI, -1.06 to -0.40); when it was resistance training, HbA1c fell by 0.57 (95% CI, -1.14 to -0.01).²¹ Simply advising a patient to be physically active—without involvement in both the planning and supervision—led to statistically significant reductions in HbA1c only when the advice was combined with dietary recommendations. Giving patients both exercise advice and dietary recommendations led to an HbA1c reduction of 0.58 (95% CI, -0.74 to -0.43).²¹

The duration of the structured exercise mattered, too, of course, with those who ex-

ercised more than 150 minutes per week achieving a larger reduction in HbA1c than those who exercised 150 minutes or less (-0.89; 95% CI, -1.26 to -0.50 vs -0.36; 95% CI, -0.50 to -0.23). Higher intensity activity did not improve glycemic control any more than moderate intensity exercise.²¹

Mind-body stress relievers

The National Health Interview Survey (NHIS) estimated that in 2007 (the most recent survey that addressed mind-body modalities), 19% of US adults used at least one mind-body modality in the previous 12 months.²² Modalities included in the NHIS were biofeedback and yoga, body interventions best studied for diabetes management. Here's what the evidence shows:

■ **Biofeedback.** In a small RCT (N=30 patients with T2DM) comparing biofeedback-assisted relaxation training (10 weekly 45-minute sessions) with education alone, the treatment group had significant improvement in HbA1c levels (which went from 7.4% to 6.8%) and in average blood glucose values that persisted at 3-month follow-up.²³

Biofeedback can also produce clinically significant toe temperature elevations. In patients with T2DM, volitional warming has been associated with increased circulation, improvement or elimination of intermittent claudication pain, more rapid healing of diabetic ulcers, and improved functional status.²⁴

■ **Yoga.** Two systematic reviews concluded that yoga is likely to benefit patients with T2DM, leading to lower blood sugar, LDL-C levels, triglycerides, body weight, waist-to-hip ratio, and HbA1c, and higher HDL-C.^{25,26} Additionally, yoga appears to have a beneficial effect on the blood pressure, heart rate, oxidative stress, sympathetic activation, catecholamine levels, coronary stenosis, coagulation profiles, and pulmonary function of patients with T2DM, and is associated with reductions in the amount of medication needed and in psychosocial risk factors. (Because of the heterogeneous nature of the studies reviewed, however, no statistical analyses were reported.)

A third systematic review, which included only 5 studies, found that yoga yielded a short-term improvement in FBG and lipids, but no statistically significant improvement in long-term outcomes of body mass index, body weight, or HbA1c.²⁷ All 5 studies noted that there were methodological problems and uncertainty about the generalizability of the findings to Western culture.

■ **Meditation.** The regular practice of transcendental meditation (TM) is associated with a reduction of catecholamine levels, a study comparing meditators with a control group found.²⁸ A study examining the relationship between depression and diabetes found compelling evidence of an association between mental stress and hypothalamic-pituitary-adrenal axis hyperactivity,²⁹ and another comparing meditators with controls found the regular practice of TM to be associated with a reduction in catecholamine levels.³⁰ As increased catecholamine levels affect glucose transport and insulin resistance, this finding suggests that reducing stress levels through meditation might lead to improved glycemic control.

One RCT comparing diabetes education alone with education plus stress management (progressive muscle relaxation, deep breathing, and mental imagery) found that HbA1c levels decreased by 0.5 in the latter group at one year.³¹ In a single blinded randomized study, the TM group had a statistically significant reduction in mean arterial pressure, insulin resistance, and insulin levels compared with those who received diabetes education alone.³²

■ **Qigong.** The effectiveness of Qigong systems such as Tai Chi—which integrate physical postures, breathing techniques, and focused attention—is difficult to determine because of methodological challenges in design and variability in practice. Authors of a systematic review of Tai Chi and diabetes found only 2 RCTs and 3 nonrandomized clinical trials and concluded that there was no convincing evidence that the practice aids in glucose control.³³ Two other systematic reviews of Qigong for T2DM reported some improvement in glucose control, but limited study quality prevented definite conclusions.^{34,35}

When to consider “manual medicine”

An integrative approach to health also includes a number of modalities collectively known as manual medicine: acupuncture, massage/energy therapy, acupressure, and chiropractic and other forms of manipulation. Evidence on these modalities for the treatment of diabetes and diabetic complications is limited.

■ **Acupuncture.** Although acupuncture has long been reported to improve glycemic control in patients with diabetes and prediabetes, the evidence is limited and of poor quality.^{36,37}

In recent years, 2 small RCTs have found that acupuncture reduced pain in patients with diabetic peripheral neuropathy vs sham acupuncture or oral inositol.^{38,39} In one of the studies, 87.5% of participants randomized to acupuncture had symptom improvement, compared with 63.6% of those in the oral inositol group. In fact, marked symptom relief after 3 months of treatment was reported by 50% of those who had acupuncture, compared with 21% of those who did not.³⁹

In a small 2-week RCT, patients randomized to acupuncture vs sham acupuncture for diabetic bladder dysfunction showed statistically significant improvements in both subjective symptoms and urodynamic measurements.⁴⁰ And a study comparing patients receiving electroacupuncture—in which an electric current is transmitted between 2 needles placed in the muscles—vs sham acupuncture found nonstatistically significant improvements in symptomatic gastroparesis.⁴¹

■ **Massage/energy therapy.** Massage has been shown in several studies to reduce glucose levels,⁴²⁻⁴⁴ although no reductions in glucose levels were found in one small RCT.⁴⁵ Connective tissue reflex massage led to improved lower limb blood flow in patients with diabetes and peripheral artery disease in another study, but the clinical significance is uncertain.⁴⁶ Studies of reflexology and acupressure are similarly limited to small experimental and observational studies.⁴⁷ No RCTs of chiropractic treatment for diabetes were found.



Transcendental meditation has been found to reduce mean arterial pressure, insulin resistance, and insulin levels.

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