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Improving the Scientific Rigor of Nutritional Recommendations for Adults with Diabetes:

A Comprehensive Review of the American Diabetes Association Guidelines Recommended Eating Patterns

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Abbreviations:

ADA, American Diabetes Association; **2018 Standards**, Standards of Medical Care in Diabetes - 2018; **2014 Recommendations,** Nutrition Therapy Recommendations for the Management of Adults with Diabetes - 2014; **DASH**, Dietary Approach to Stop Hypertension; **RCTs**, Randomized Controlled Trials; **T2D**, type 2 diabetes; **T1D**, type 1 diabetes; **CVD,** cardiovascular disease; **BMI**, body mass index; **HDL-C**, high density lipoprotein cholesterol; **GI,** Glycemic Index

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INTRODUCTION

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Over half of adult Americans now have diabetes or prediabetes[1] and worse, this epidemic is now world-wide and shows no signs of slowing, with rates of both diabetes and diabetes-related health complications still rising.[2] When advising patients with diabetes on food choices, many providers rely on nutrition guidelines provided by the American Diabetes Association (ADA), and these guidelines influence other recommendations across the globe. Given the alarming trends in diabetes,[2] it is paramount to review the treatment guidelines to ensure they are based on rigorous and accepted scientific methods. Our review included the evidence cited by the ADA in support of its claims and recommendations for eating patterns to combat diabetes (see Description of Eating Patterns, Supplemental Appendix), as presented in the most current edition of the annual ADA's Standards of Medical Care in Diabetes (2018 Standards).[3] Our review also includes sources cited in the latest edition of the ADA's Nutrition Therapy Recommendations for Adults with Diabetes (2014 Recommendations),[4] which also informed the 2018 Standards. In October 2018 low carbohydrate was named as a recommended eating pattern by the ADA and European Association for the Study of Diabetes (EASD)[5] but only citations from the 2014 and early 2018 ADA documents were reviewed.

METHODS

In our review, we evaluated each study cited in the eating pattern section and all studies related to low carbohydrate diets in the 2014 Recommendations and the 2018 Standards. We sought to identify if each study was appropriate for inclusion in the guidelines using defined criteria. The criteria were created to ensure that each study could be used to evaluate the "cornerstone" of diabetes management which the ADA defines as metabolic control. The decision to include only clinical trials eliminated all prospective cohort studies from the inclusion list. While some prospective cohort studies may be appropriate in the prevention section of the guidelines, their conclusions are not appropriate for the nutrition therapy section as there is no specific intervention being tested, and therefore cannot be used to evaluate metabolic control. We considered glycemic control to be the primary biomarker for metabolic control in diabetes management, and additionally reported all available lipoprotein and blood pressure data. Additionally, we searched the literature for other articles that might be appropriate for consideration in the development of dietary guidelines for diabetes utilizing the search terms DASH, Mediterranean, vegetarian, vegan, plant-based, low carbohydrate, and ketogenic along with diabetes. The search was limited to human studies published in English through May 30, 2018. An algorithm for each eating pattern search can be found in Supplemental. Each study, either cited by the ADA or identified in our searches, was evaluated via the following criteria to be considered appropriate for inclusion in the guidelines: 1) It was a clinical trial, or a systematic review or systematic review/meta-analysis of clinical trials; 2) It involved participants with type 1 diabetes (T1D) or type 2 diabetes (T2D); 3) One of the study arms followed one of the three eating patterns recommended by the ADA or a low-carbohydrate diet; 4) Its reported outcomes included glycemic control; 5) outcomes were reported separately for participants with diabetes if a sub-group analysis of a larger trial. The searches were done twice by two different coauthors to ensure that all relevant studies were captured and reviewed, and to decrease the risk of bias. The results of the two searches were then combined and are presented in the Supplemental tables 1-4. If there was not consensus about the appropriateness of inclusion for a particular study between the two coauthors, a third coauthor reviewed and made the final decision about inclusion or exclusion.

The aim of this critical review was not to assign a grade to a particular study per se, but rather to determine the strength of grading by the ADA. The evidence for eating patterns was chosen to be reviewed as it was assigned a Grade E (expert opinion) by the ADA without describing how the studies they chose to cite were selected or reviewed, or how the experts had weighted various endpoints in forming their opinion. This lack of this rigor leaves readers to rely on the expert opinion provided to be free from bias and in line with the available literature. The concern raised in this critical review is that this may leave readers uninformed and unable to form their own opinion regarding what nutrition recommendations may be best for their patients. For example, many of the studies cited for the eating patterns in the guidelines intended specifically for patients with diabetes, did not have glycemic control as an end point; for the DASH eating pattern, this was the vast majority of the studies cited. Given the central importance of glycemic control in managing patients with diabetes, this leaves providers without sufficient direction. Our review and presentation of the evidence will enable the reader to assess for themselves the totality of the evidence. To this goal, we have created three sets of tables with varying degree of detail. This also can be used in the creation of future iterations of the ADA guidelines.

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Table 1 Summary of evaluation of studies on different eating patterns cited in the ADA 2018 guidelines and 2014 Nutrition Recommendations

Study #	ADA Statement/ Recommendation	Citation	Study Type	Description	Subjects	Duration	Findings for DASH Diet	Comments
DASH DIET								
1	"A variety of eating patterns (combinations of different foods or food groups) are acceptable for the management of diabetes. ...In one small study in people with type 2 diabetes, the DASH eating plan ... improved A1c, blood pressure, and other cardiovascular risk factors." (46)	Azadbakht L, 2011 [ref 46, ADA 2014]	Randomized crossover	Compared DASH diet to control diet. Calorie and macronutrient distribution same in both. **No information given about baseline diet and both groups lost weight.**	**n=44 persons** with T2D; 31 (70%) completed.	8 weeks each diet	♦ **HbA1c** ↓20.8% **BG SS** ♦ **FBG** ↓18.3% **BG SS** ♦ **Weight loss** ↓6.8% **BG SS** ♦ **HDL**↑ **BG SS** ♦ **SBP, DBP** ↓**BG SS** **TRG** ↑	**Should be included in a review of the evidence.** Supports statement. *Error in reporting and analysis of triglycerides
2	"The blood pressure benefits are thought to be due to the total eating pattern, including the reduction in sodium and other foods and nutrients that have been shown to influence blood pressure." (99, 105)	Harsha DW, 1999 [ref 99, ADA 2014]	RCT	Multi-center DASH trial. Compared control diet (typical fat content for Americans); diet rich in fruit and vegetables; DASH (fruit, vegetables, low fat)	n=459 persons with BP <160mmHg systolic, 80-95mmHg diastolic	8 weeks	No data on persons with diabetes	**Should not be included in review of evidence.** This study excluded subjects with significant disease. Study does not include analysis of subjects with T2D.
3		US HHS, USDA Dietary Guidelines for Americans, 2010 [ref 105, ADA 2014]	Health policy report	Diet recommendations for the general population; includes sodium limit for blood pressure control.				**Should not be included in a review of the evidence.** DGAs are not intended for persons with diabetes.
4	"In people without diabetes, the DASH eating plan has been shown to help control blood pressure and lower risk for CVD and is frequently recommended as a healthful eating pattern for the general population (104–106). ... Limited evidence exists on the effects of the DASH eating plan on health outcomes specifically in individuals with diabetes; however, one would expect similar results to other studies using the DASH eating plan."	Sacks FM, 2001 [ref 104, ADA 2014]	RCT	Compared DASH and control diets (typical US diet). Within each group, participants ate foods with high, mid, and low sodium for 30 days each, in random order.	n=412 (SBP 120-159mmHg; DBP 80-95mmHg) 95% completed	8 weeks	No data for persons with diabetes	**Should not be included in a review of the evidence.** Study does not include separate analysis of participants with T2D.

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5		Appel L, 1997 [ref 106, ADA 2014]	RCT	Compared effects of varied sodium levels in control, fruit and vegetable-rich diet and DASH (fruit + veg, low fat)	n=459 persons with SBP 160mmHg DBP 80-95mmHg	8 weeks	No data on persons with diabetes	**Should not be included in review of evidence.** Study does not include separate analysis of subjects with T2D.
6	The DASH diet is an example of a healthful eating pattern that have shown positive results in research. (56-58)	Cespedes EM, 2016 [ref 56, ADA 2018]	Observational data analysis from an RCT (Women's Health Initiative)	Investigated incidence of T2D in adherents of 4 dietary patterns including DASH	n=101,504		Lowest incidence of T2D associated with adherence to DASH.	**Should not be included in review of evidence.** This may belong in the prevention section but not appropriate in the management section.
7		Ley SH, 2014 [ref 57, ADA 2018]	Non-systematic review; included 2 prospective studies on DASH	2 studies on DASH based on food intake reports and T2D incidence.			DASH associated with lower T2D risk.	**Should not be included in review of evidence.** It is not a systematic review and no additional studies cited.
8		Campbell AP, 2017 [ref 58, ADA 2018]	Commentary	Presents basics of DASH diet and DASH studies, including one RCT in persons with T2D				**Should not be included in a review of the evidence.** This was a commentary not based on a systematic review only one study on persons with T2D was mentioned.
MEDITERRANEAN DIET								
1	The Mediterranean diet improves glycemic control, weight, lipids and other CVD risk factors in persons with diabetes. (11,72,83,88,100)	Esposito, 2009 [ref 72, ADA 2014; ref 54, ADA 2018]	RCT	Tests diet for efficacy in delay of medication initiation in newly diagnosed patients. Med "low carb" diet (<50%E CHO) vs. control diet (<30%E fat). Both diets were calorie restricted.	**n = 215** overweight persons newly diagnosed with T2D	4 years	♦ **HbA1c** Y4: $\downarrow$12.8% BG SS ♦ **HDL, TRIG, weight** Superior to control nSS Y4 **% requiring meds at Y4** **Med diet:** 44% **Control:** 70%	**Should be included in a review of the evidence.** Supports statement with limitations: Some benefits not sustained. 44% required medication by end of study.
2		Estruch, 2013 [ref 83, ADA 2014]	RCT PREDIMED study ****Has been retracted and replaced**	CV events was main outcome of interest. Compared 2 versions of Med diet to low-fat control diet. Not calorie restricted.	**n=3614** with diabetes	4.8 years	The two Med diets reduced rate of absolute risk reduction low SS for only stroke.	**Should be included in a review of the evidence**. Supports statement on CVD risk but retraction and replacement are a limitation of evidence.
3		Elhayany, 2010 [ref	RCT	Compared low-carbohydrate Med diet,	**n=259** with T2D	12 months	♦ **HbA1c** ♦ Low-carb Med $\downarrow$24.1%	**Should be included in a review of the**

		100, ADA 2014]		traditional Med diet, and 2003 ADA diet. Limited to 20 calories/kg body weight in all study groups. Main outcomes: HbA1c, FBG, triglycerides.			BG SS Trad Med ↓21.7% BG SS ♦ **Weight loss** ♦ Low-carb Med ↓10.3% BG SS Trad Med ↓8.7% BG SS ♦ **HDL, LDL and TRIG** Med diets were superior.	**evidence**. Supports statement Macronutrient composition may influence efficacy.
4		Wheeler, 2013 [ref 88, ADA 2014]	Systematic review	2001-2010 review on diet and diabetes; included 7 studies on Med diet		4 weeks to 4 years	“There are mixed results for CVD risk factors with some studies indicating that the Mediterranean-style eating pattern might improve HDL cholesterol and TG."	**Should be included in a review of the evidence.** Does not strongly support the statement.
5		Franz, 2010 [ref 11, ADA 2014]	Systematic review	Review of the evidence for the ADA's nutrition practice guidelines. Includes 2 RCTs, notes inadequacy of 2 cross-sectional and 1 case-control study. Main outcomes: peripheral artery disease risk, diabetes risk and intake of foods defining the Med diet; CVD risk	Persons with diabetes or other CVD risk factors		Notes that the Med diet has shown benefit for endothelial health, blood pressure and lipid levels, but concludes that "a clearer understanding is needed" of the diet's "protective mechanisms and role in diabetes management."	**Should be included in a review of the evidence.** Does not strongly support ADA statement.
6	A variety of eating patterns are acceptable for persons with diabetes. The Mediterranean diet is an example. (54,55)	Boucher, 2018 [ref 55, ADA 2018]	Commentary based on non-systematic review	Discussions of select studies on the Med diet in diabetes				**Should not be included in a review of the evidence.** This was a commentary not based on a systematic review.
PLANT-BASED DIET								
1	A variety of eating patterns are acceptable for the management of diabetes. Plant-based diets (59, 60) are an example of a healthy eating pattern.	Rinaldi S, 2015 [ref 59, ADA 2018]	A non-systematic review	Lit search thru March 2015. Reviewed 13 studies (5 original RCTs, 4 observational, 3 FU or ancillary to RCT, 1 meta-analysis) on glycemic control, CVD risk, other health measures			Results mixed on efficacy of PBD for glycemic control, weight loss, CVD risk improvement Limitations: Of 5 RCTs, 2 had n < 20, short duration (4, 12 weeks).	**Should not be included in a review of the evidence.** not a systematic review

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2		Pawlak R, 2017 [ref 60, ADA 2018]	Commentary based on non-systematic review	Reviews observational studies on diabetes				**Should not be included in a review of the evidence** This was a commentary not based on a systematic review.
3	Six plant-based diets reviewed found inconsistent results for glycemic control and weight loss. "Diets often did result in weight loss (36, 93, 101-103,131). More research on vegan and vegetarian diets is needed..."	Barnard N, 2006 [ref 36, ADA 2014]	RCT	Compared low-fat vegan diet to ADA diet for glycemic control and CVD risk. Only the control diet was E-restricted.	**n=99** with T2D	22 weeks	♦ **HbA1c** ↓11.3% **WG SS; BG nSS** ♦ **FBG** ↓21.7% **WG SS, BG nSS** ♦ **Weight loss** ↓6.1% **WG SS, BG nSS** ♦ **Diabetic meds** ↓43% **BG SS** ♦ **HDL↑ LDL↓ VLDL↓ TRG↓** All **WG SS**, **BG nSS**	**Should be included in a review of the evidence.** Supports statement that results for diet are inconsistent.
4		Turner-Grievy G, 2008 [ref 93, ADA 2014]	Nutritional assessment of diets tested in Barnard, 2006 trial	Ancillary study to 22-wk. trial (Barnard, 2006). Assessed changes from baseline of nutrient intake and diet quality of participants, using metric based on the US DGA			Increased intakes of CHO, fiber, some micronutrients and improved AHEI score; ADA diet group AHEI score stayed same.	**Should not be included in a review of the evidence.** The DGA are not to be applied to persons with diabetes.
5		Nicholson A, 1999 [ref 101, ADA, 2014]	RCT	Compared non-isocaloric low-fat vegan and low-fat diets on glycemic control and CVD risk factors. **LFV prepared meals lowered in E** than those for LF meals.	**n=13** with T2D, 11 completed	12 weeks	♦ **HbA1c**↓16.9% **BG nSS** ♦ **FBG**↓27.7% **BG SS** ♦ **Weight loss** 7.4% > **BG SS** **Lipids** all **nSS** **Control arm had 4 participants**	**Should be included in a review of the evidence.** Supports some statements No glycemic advantage over control.
6		Tonstad S, 2009 [ref 102, ADA 2009]	Cross sectional	Assessed prevalence of T2D in the Adventist Health Study cohort on different types of vegetarian diets and in nonvegetarians	1007 in sub-group analysis of health measures; n with T2D unstated		**T2D prevalence** Vegans 2.9% OR .51 prevalence in vegans Nonvegetarians 7.6% T2D=diagnosed or FBG ≥126mg/dl **BMI** Vegans 23.6 (lowest of all diet types) Nonvegetarians 28.8	**Should not be included in a review of the evidence** Observational studies cannot provide evidence for treatment efficacy.

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7		Kahleova H, 2011 [ref 103, ADA 2014]	RCT	Compared E-restricted vegetarian and conventional diabetic diets on body fat, IS, oxidative stress. No exercise for first 12 weeks and then exercise added in second 12 weeks.	**n=74** with T2D	24 weeks	♦ **HbA1c** ↓8.6% **BG nSS** ♦ **Weight loss** ↓6.1% **BG SS** ♦ **Medication** ↓43% **BG SS** ♦ **LDL ↓WG SS, BG nSS** **Oxidative stress markers improved more in experimental arm** **HDL, TRG nSS but TRG increased only in experimental**	**Should be included in a review of the evidence.** Supports some statements Improvements in weight, oxidative stress and medication in experimental group. Triglycerides increased in plant-based diet.
8	Plant-based diets often result in weight loss	Barnard N, 2009 [ref 131, ADA, 2013]	F-U to RCT	Compared low-fat vegan and ADA diets for glycemic control and CVD risk. 74-week FU to 22-week RCT (Barnard, 2006)	**n=99** with T2D	74 weeks	**HbA1c** ↓2.5% **WG, BG nSS** **Weight loss** ↓4.5% **WG SS, BG nSS** **LDL**↓ **VLDL**↓ **TRG**↓ All **WG SS, BG nSS**	**Should be included in a review of the evidence.** Supports some statements
LOW CARBOHYDRATE STUDIES								
1	See below - statements 1, 3, 7, 8, 9,10	Stern L, 2004 [ref 92, ADA 2014]	Follow-up	1-yr FU to 6-mo RCT in which patients followed either low-carbohydrate diet or cal-restricted (-500 cal/day) low-fat diet.	**n=54** obese adults with T2D; 34 (63%) completed study (subgroup of larger study cohort).	1 year	♦ **HBA1c** ↓10.8% **BG SS** **FBG BG nSS** **Insulin resistance BG nSS** Lipid levels not reported for T2D subgroup.	**Should be included in a review of the evidence.** Supports statements 1 and 3. Refutes statements 7, 8, 9 and 10
2	See below - statements 1, 4, 7,8,9, 10	Elhayany A, 2010 [ref 100 in ADA 2014]	RCT	Compared low-carbohydrate Med diet, traditional Med diet, and 2003 ADA diet. All diets restricted calories to 20/kg. of body weight.	**n=259** overweight or obese adults with T2D; 194 (75%) completed.	1 year	♦ **HbA1c** ↓24.1% **BG SS** ♦ **FBG** ↓41.3% **BG SS** **Weight Loss** ↓10.3% **BG nSS** **HOMA** ↓28.9% **BG nSS** ♦ **HDL-C** ↑ only with low-carb Med diet. ♦ **TRG** ↓ greatest on low-carb diet **BG SS**	**Should be included in a review of the evidence.** Supports statements 1 and 4. Refutes statements 3,7,8, 9 and 10

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3	See below - statements 1, 3, 4,9,10	Miyashita Y, 2004 [ref 107, ADA 2014]	RCT	Compared effects of low-carbohydrate diet vs. high-carbohydrate diet on glucose and lipid metabolism, especially visceral fat accumulation.	**n=22** obese adults with T2D; n completed unknown.	4 weeks	♦ **Fasting insulin** ↓30% **BG SS** ♦ **HDL** ↑15% **BG SS** ♦ **FBG** ↓50.0% **BG nSS** **Weight Loss** ↓12.3% **BG nSS**	**Should be included in a review of the evidence**. Supports statements 1, 3, 4,9,10 Limitation: carb intake unknown.
4	See below - statement 1, 3, 7,8,9,10	Shai I, 2008 [ref 108, ADA 2014]	RCT	Compared safety and effectiveness of 3 diets (low-fat, restricted-calorie; Mediterranean, restricted-calorie; low-carbohydrate, not restricted-calorie) in obese persons, some with T2D.	322 obese adults, **n=46** (14%) with T2D. Data for only 36 participants with T2D available for statistical analysis (low-carb n=12, Med n=13, low-fat n=11).	2 years	♦ **HbA1c**: Low fat decrease 0.4 Mediterranean decrease 0.5 Low carb decrease 0.9 **FBG** better in Mediterranean **HOMA-IR** better in Mediterranean	**Should be included in a review of the evidence.** Supports 1, 3 Refutes statement 7,8,9,10
5	See below - statements 1, 3, 4, 7, 8, 9, 10	Jonsson T, 2009 [ref 109, ADA 2014]	RCT crossover	Compared Paleolithic diet vs. ADA diabetes diet for improving CVD risk.	**n=13** adults with T2D; 100% completed.	3 months on each diet	♦ Improved glycemic control and CVD risk factors - HbA1c, TRG, DBP, HDL, weight loss **BG SS**	**Should be included in a review of the evidence.** Supports statements 1, 3, 4,9, 10 Refutes statement 7,8
6	See below - statements 1, 3, 5	Khoo J, 2011 [ref 110, ADA 2014]	RCT	Compared effects of two diets (low-calorie vs. low-calorie/high protein/low- fat) on weight loss, sexual and endothelial function, lower urinary track symptoms, and inflammatory markers in obese men.	31 obese men with T2D (% completed unknown).	8 weeks	**Not relevant**	**Should not be included in a review of the evidence.** Does not provide data on any outcomes addressed in statements.
7	See below - statements 2, 5, 7, 8, 9,10	Davis NJ, 2009 [ref	RCT	Compared the effects on weight loss and glycemic control of a	**n=105** overweight adults with	1 year	**HBA1C** At 3 mos. ↓8.0%	**Should be included in a review of the evidence.**

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		71, ADA 2014]		low-carbohydrate diet vs. low-fat diet in adults with T2D.	T2D (% completed unknown).		At 1 year returned to baseline. **BG nSS** **WEIGHT LOSS** Both groups lost 3.4% at 1 yr. **SBP, DBP, LDL, HDL, TRG:** no SS results. **Insulin reduced in low-carbohydrate arm and increased in control**	Limited support for statement 2 but meds reduced more in low-carbohydrate arm. Supports statement 5. Refutes 7, 8, 9, 10
8	See below - statements 2, 3, 4	Daly ME, 2006 [ref 112, ADA 2014]	RCT	Compared low-carbohydrate diet vs. reduced-portion, low-fat diet.	**n =102** obese adults with poorly controlled T2D; 79 (77.5%) completed.	3 months	♦ **HbA1c** ↓6.1% **BG nSS** ♦ **Total C:HDL ratio** Improved most in low-carb diet **BG SS** **Medications reduced more in low-carbohydrate arm**	**Should be included in a review of the evidence.** Limited support for statement 2 but meds reduced more in low-carbohydrate arm. Supports statement 4 Refutes and supports part of statement 3.
9	See above - statements 2, 3, 5, 10	Dyson PA, 2007 [ref 113, ADA 2014]	RCT	Assessed the impacts on body weight, HbA1c, ketone and lipid levels in diabetic and non-diabetic subjects, comparing low-carb diet (≤ 40 g/day) vs. a calorie-restricted diet based on UK diabetes diet.	**n=13** overweight or obese adults with T2D and 13 adults without T2D; 12 (92.3%) with T2D completed the study.	3 months	**HbA1c ↓5.5% BG nSS** ♦ **Weight loss** ↓6.9kg **BG SS** **Lipids (HDL, total C, LDL, TRG): BB nSS**	**Should be included in a review of the evidence.** Supports statements 2, 3, 5, 10.
10	See below - statement 1, 4, 10	Kirk JK, 2008 [ref 115, ADA 2014]	Systematic review/ meta-analysis	Reviewed 13 studies on carbohydrate-restricted diets for adults with T2D (RCT, crossover; RCT parallel; non-randomized two-arm; single-arm pre-post).	Adults with T2D. Study n range: 8-52.	1 week to 26 weeks	**HbA1c** 1 study ↑2.7%; 1 study 0% change; 9 studies ↓3.7%-22.4%. Of 6 studies with data for both low-carb and high-carb, low-carb performed better in 4.	**Should be included in a review of the evidence.** Some support for statement 1, 4, 10
11	See below - statement 3, 5, 9, 10	Iqbal N, 2010 [ref	RCT	Compared effects of low-carbohydrate diet	**n=144** OB adults with T2D; 68	2 years	**HbA1c** ♦ At 6 mos. ↓6.3%	**Should be included in a review of the evidence.**

		116, ADA 2014]		vs. low-fat, calorie-restricted diet	(47.2%) completed.		**BG SS** At 2 years ↓2.6% **BG nSS** **FBG** At 2 years ↓1.3% **BG nSS** **Weight loss** At 2 years ↓1.3% **BG nSS** ♦ **TRG** ↓26 mg/dl (16.8%) All other lipids nSS	Supports statement 3, 5, 9, 10.
12	See below statement 1, 3, 8	Wheeler ML, 2010 [ref 72, ADA 2018]	Systematic review	2001-2010 review on diet and diabetes; included 11 studies on low-carbohydrate diets.	n range=10-55 per study group	2 weeks to 1 year	HbA1c decreased with a low-carb diet in 6 of 10 studies. Of the 4 other studies, 3 had tested a very-low-carb diet and 1, a moderately low-carb diet. ♦ **FBG, 24-hour insulin, fasting insulin and insulin sensitivity** improved "significantly on the lower-carbohydrate diet." ♦ **Need for diabetes medication** lower with lower-carb diets. Some studies showed lower-carb diets improved lipid levels, most notably HDL and TRG. **Conclusion:** Evidence mixed and of not high quality due to study size, duration, dropout rates, or lack of randomization in some cases.	**Should be included in a review of the evidence with clarification:** 1) very low-carb is mis-defined as ≤70g/day; 2) does not distinguish outcomes data by reported carb consumption. Of the 7 trials categorized as very low-carb, reported carb consumption was <70g/day for only 3 trials (all three attained a SS improvement in HbA1c, -6.8% to -17%). Supports statements 1, 3, 8
13	See below statement 9	Snorgaard O, 2017 [ref# 74, ADA 2018]	Systematic review and meta-analysis	Review/analysis of 10 RCTs to address the question: Is there an ideal amount of dietary	pooled n=1376	varied	The ideal amount of carbohydrates in the diet in the management of T2D is unclear.	**Should be included in a review of the evidence**.

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				carbohydrate for individuals with T2D? Analyzed association of reported carbohydrate intake with reduction in HbA1c.			Low-carbohydrate and moderate-carbohydrate diets have greater glucose-lowering effect compared with high-carbohydrate diets. **The greater the carb restriction, the greater glucose lowering.** Apart from improvements in HbA1c over the short term, low-carbohydrate is not superior to high-carbohydrate for glycemic control or weight.	Supports statement 9.
14	See below statement 9	van Wyk HJ, 2016 [ref 75, ADA 2018]	Review	Aimed to better understand efficacy of low-carbohydrate diets for glycemic control as well as the reasons for different conclusions among 9 meta-analysis on the subject. Reviewed were 12 RCTs that were ≥4 weeks and which tested low-carbohydrate diets of ≤ 45g/day,	Adults with T2D	≥ 4 wks	**Conclusions:** Variability in study design and subject characteristics, as well as reported carbohydrate intake, may account for differences in studies' findings; total E intake is the best predictor of body weight; low-carbohydrate diets perform no better than high-carbohydrate diets to improve metabolic markers; very low-carbohydrate diets may not be sustainable, as carb intake often returns to a more moderate level over time.	**Should be included in a review of the evidence, but with clarification:** Supports statement 9 It was likely adherence, not the low-carb diet per se, that determined outcomes. Reported carbohydrate intake at end of study for low-carb arms, for the 12 studies, was 132-228 g/day.
15	See below statement 1, 4, 9	Meng Y, 2017 [ref 76, ADA 2018]	Systematic review and meta-analysis	Reviewed 9 RCTs; aimed to assess the efficacy of low-carbohydrate diets compared to normal/higher-carbohydrate, low-fat diets in T2D.	Pooled n=734 adults with T2D	3-24 months	♦ Superior benefit for HbA1c, TRG, HDL, and short-term weight loss, but not LDL, total cholesterol, FBG or long-term weight loss, when compared to control diet.	**Should be included in a review of the evidence.** Supports statement 1, 4, 9 **Limitation:** Analysis did not consider reported carbohydrate intake

								of study diets but only target levels.
16	See below statement 2, 3, 4, 8, 9, 10	Tay J, 2015 [ref 77, ADA 2018]	RCT	Compared effects of a very low-carb, high-unsaturated fat/low-saturated fat diet vs. a high-carbohydrate, low-fat diet on glycemic control and CVD risk factors in T2D. Calories restricted for both study arms.	**n=115** overweight or obese adults with T2D; 77 (68.0%) completed.	1 year	♦ **HbA1c** ↓13.7% **BG nSS** **FBG** ↓9.0% **BG nSS** **Weight loss** ↓9.6% **BG nSS** Conclusion: Weight loss, not macronutrient composition, was the primary determinant of weight loss. ♦ Blood glucose stability, HDL, TRG were SS improved. **More medication reduction in low-carbohydrate arm**	**Should be included in a review of the evidence.** Supports statement 4 but more med reduction in low-carbohydrate arm. Refutes and supports part of statement 3. Supports statement 4 Refutes statement 8, 9, 10
17	See below statement 10	Goday A, 2016 [ref 78, ADA 2018]	RCT	Evaluated the short-term safety and tolerability of a very low-carbohydrate, ketogenic diet (<50g/day) in a weight loss /lifestyle modification program for adults with T2D. VLCK group ate commercial weight-loss products and natural foods. Low-calorie control diet was based on ADA guidelines.	**n=89** obese adults with T2D; 76 (85.4%) completed.	4 months	**Safety** No SS differences in safety parameters were found between the two study groups, including: **Urinary albumin-to-creatinine ratio, estimated glomerular filtration rate, Creatinine and blood urea nitrogen**: no SS changes from baseline or BG. **Sodium, potassium, chloride, calcium and magnesium:** remained stable and within the normal limits in the two study groups at all time points. No serious adverse events were reported, and mild AE in the VLCK diet group declined at last follow-up. **Efficacy**	**Should be included in a review of the evidence.** Supports statements 1, 5 Refutes and supports parts of statement 3. Refutes 7, 8 However, it is not sufficient support for the claim. Other studies (see Table 8) provide safety data from longer studies.

							♦ **HbA1c** ↓13.0% **BG SS** ♦ **FBG** ↓20.5% **WG SS BG nSS** ♦ **HOMA-IR** ↓49.3% **BG SS** ♦ **TRG** ↓23.9% **WG SS BG nSS**	
18.	See below statement 1, 3, 4, 7, 8, 10	Saslow L, 2017 [ref 79, ADA 2018]	RCT	Compared effects on glycemic control and other outcomes of 2 online interventions (ad libitum very low-carbohydrate with behavioral support vs. ADA's “Create Your Plate” diet.	**n=25** overweight adults with T2D; 18 (72%) completed.	32 weeks	♦ **HbA1c** ↓11.3% **BG SS** ♦ **Weight loss** ↓11.6% **BG SS** ♦ **TRG** ↓34.5% **BG SS** **HDL, LDL:** no SS changes	**Should be included in a review of the evidence.** Supports statements 1, 4, Supports and refutes parts of statement 3 Refutes statement 7, 8
19.	See below-statement	Wolever, 2008 [ref 14 in ADA 2014]	RC	Aim was to compare the effects of altering the GI or the amt of carbohydrate on HbA1c, FBG, and other biomarkers. Compared 3 diets: High-carbohydrate, high GI High-carbohydrate, low GI Lower carbohydrate, high monounsat-fat	**n=162**	12 months	**HbA1c: At 12 mos was identical for the 3 groups**	**Should not be included in a review of the evidence.** Carbohydrate intake was moderate, not low.

ADA statements: 1) "Some published studies comparing lower levels of carbohydrate intake (ranging from 21 g daily up to 40% daily energy intake) to higher carbohydrate intake levels indicated improved markers of glycemic control and insulin sensitivity with lower carbohydrate intakes (92, 100, 107-111)."
2) "Four RCTs indicated no significant difference in glycemic markers with a lower-carbohydrate diet compared with higher carbohydrate intake levels (71, 112-114)."
3) "Many of these studies were small, were of short duration, and/or had low retention rates (92,107, 109,110,112,113)."
4) "Some studies comparing lower levels of carbohydrate intake to higher carbohydrate intake levels revealed improvements in serum lipid/lipoprotein measures, including improved triglycerides, VLDL triglyceride, and VLDL cholesterol, total cholesterol, and HDL cholesterol levels (71,92,100,107,109,111,112,115)."
5) "A few studies found no significant difference in lipids and lipoproteins with a lower-carbohydrate diet compared with higher carbohydrate intake levels. It should be noted that these studies had low retention rates, which may lead to loss of statistical power and biased results (110,113,116)."
6) "Evidence exists that both the quantity and type of carbohydrate in a food influence blood glucose level, and total amount of carbohydrate eaten is the primary predictor of glycemic response (55,114,117–122)."
7) ""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 (70,71)."
8) "The role of low-carbohydrate diets in patients with diabetes remains unclear (72)."
9) "While benefits to low-carbohydrate diets have been described, improvements tend to be in the short term and, over time, these effects are not maintained (74-77)."

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10) "While some studies have shown modest benefits of very low-carbohydrate or ketogenic diets (less than 50-g carbohydrate per day (78,79), this approach may only be appropriate for short-term implementation (up to 3-4 months) if desired by the patient, as there is little long-term research citing benefits or harm."

Abbreviations **T2D**, type 2 diabetes; **BG**, between group; **WG**, within group; **FBG**, fasting blood glucose; **SS**, statistically significant; **nSS**, not statistically significant; **DBP**, diastolic blood pressure; **SBP**, systolic blood pressure; **HDL**, high-density lipoprotein; **TRG**, triglyceride; **DGA**, dietary guidelines for American; **RCT**, randomized controlled trial; **UC**, usual care; **low-carb**, low carbohydrate; **CHO**, carbohydrate; **Med**, Mediterranean; **LDL**, low-density lipoprotein; **BMI**, body mass index; **HOMA-IR**, homeostasis model assessment of insulin resistance; **CVD**, cardiovascular disease; **PBD**, plant based diet; **FU**, follow-up; **VLDL**, very low-density lipoprotein; **LFV**, low-fat vegan; **E**, energy; **GI**, glycemic index; **total C**, total cholesterol; **OB**, obese; **VLCK**, very low calorie ketogenic; **IL-IRa**, interleukin 1-receptor antagonist,: **IL-6**, interleukin-6

RESULTS/DISCUSSION

DASH Diet

Cited evidence. The 2014 Recommendations and 2018 Standards cite eight studies [6-13] (Table 1) to support claims that the DASH (Dietary Approach to Stop Hypertension) diet is a healthy eating pattern for glycemic control, blood pressure, and other cardiovascular disease (CVD) risk factors in persons with diabetes. Research on DASH in persons with diabetes is limited: Only one[5] of the four RCTs [6-8, 13] on DASH cited by the ADA was on persons with diabetes; while weight, fasting blood glucose, blood pressure, HDL, LDL, and glycated hemoglobin (HbA1c) improved significantly, this trial was short (eight weeks), had a 30% dropout rate,[6] and a 14.4% increase in triglycerides. The other cited studies were one observational study,[12] as well as a commentary[10] and a non-systematic review, neither of which provided additional studies.[10] The USDA Dietary Guidelines for Americans was also cited, which is intended exclusively for healthy people, not those with diabetes.[9]

Additional evidence. We identified one additional RCT and a post hoc analysis of the ENCORE study,[14,15] which were published prior to the 2018 Standards (Supplemental Table S1). The RCT compared a control group with a calorie increase to the DASH arm with a significant calorie decrease. Despite this, there was no significant difference between groups for glycemic control although the DASH arm did have a greater decrease in blood pressure. The post hoc analysis reported a worsening in diabetes status in the DASH arm compared with control and DASH with exercise.

Summary of evidence: To our knowledge, clinical research on the DASH diet for diabetes management consists of two studies, of four and eight weeks duration and a post hoc analysis.[614,15] Only one of the two trials showed a glycemic improvement. According to our evaluation, the rest of the cited sources provided limited to no support for the DASH diet for people with diabetes. While evidence shows that

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the DASH diet reduces blood pressure, primarily in non-diabetic patients, the lack of evidence for glycemic control does not support a recommendation for DASH in patients with diabetes.

Mediterranean Diet

Cited evidence. The ADA documents cite six studies,[16-21] including three RCTs of longer duration,[16-18] to support claims that a Mediterranean diet can improve glycemic control and CVD risk factors and is therefore a healthy eating pattern for patients with diabetes (Table 1). The two RCTs found that the Mediterranean diet was superior to comparison diets;[16, 18] with one finding that a low-carbohydrate Mediterranean diet was superior to a traditional Mediterranean diet.[18] A third RCT found that the Mediterranean diet lowered incidence of stroke in persons with T2D, but this study has been retracted and replaced.[17] Two systematic reviews[19,20] found limited results for glycemic control but more robust data for CVD risk reduction. Also cited was a commentary favoring the Mediterranean diet which was based on a non-systematic selection of articles.[21]

Additional evidence. We identified four other studies on the Mediterranean diet worthy of consideration[22-25] (Supplemental Table S2). One RCT found that this diet improved HbA1c and BMI in postmenopausal women with T2D, but that the diet was not superior to usual care for improving blood pressure and lipids.[22] Two systematic reviews/meta-analyses[23,24] concluded that the Mediterranean diet is superior to other eating patterns for glycemic control, weight loss, lipid profile, and reduced need for diabetes medication. Lastly, a long, three-arm RCT[25] compared low-fat, low-carbohydrate, and Mediterranean diets in 322 obese patients, and data were available for 36 participants with T2D. Fasting glucose was the lowest in the Mediterranean-diet arm of the study, but HbA1c reduction was more substantial in the low-carbohydrate group after two years.

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Summary of evidence: The Mediterranean diet is the only dietary pattern with positive hard-endpoint data on CVD events, although this data comes from a single RCT[17], and the absolute risk reduction of events was minimal. Additionally, this trial has recently been retracted and although the reanalysis resulted in almost identical results, this raises doubts about its overall validity which need to be considered.[26] Data on glucose control with a Mediterranean diet are limited, however, findings of improved triglycerides and HDL-C in several studies lend support for this eating patterns for those with T2D.

Plant-based Diet

Cited evidence. The ADA documents cite eight studies in support of this diet[27-34] (Table 1). Of three RCTs,[29,31,33] none found a significant improvement in HbA1c over the control diet, although all improved over baseline, and all had more medication reduction in the experimental arm. FBG was reduced more than the control diet in one study, which only had four participants in the control arm and a lower calorie content for the vegan diet.[31] Additionally, a follow-up[33] to one RCT[29] found a substantial decline in benefits occurring between 22 weeks and 74 weeks.[34] The 2018 Standards cited a review by Rinaldi et al.[26] favorable to plant-based diets. The six trials reviewed did not consistently show improvements in glycemic control, weight loss, or CVD risk factors.[31-33,35-37]

Additional evidence. We identified nine studies[36-44] not included in the ADA review, two of which were published after the 2018 Standards (Supplemental Table S3). Of the three RCTS found, two reported significant improvements in glycemic control[36,40] in the plant-based arm and one did not.[38] However, it is important to note that triglycerides increased in the intervention arm in all three trials. A randomized crossover trial found a low glycemic index (GI) but high-carbohydrate diet produced lower insulin and glucose response after a meal compared to a higher fat, high GI diet.[44] A follow-up study[39] to the 2011

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Kahleova trial[33] found that significant improvements (from baseline) made initially to HbA1c had been lost. A single-arm demonstration study[41] found a plant-based diet, coupled with digital support, was effective for glycemic control, according to patient-reported outcomes on HbA1c, and another non-randomized study found no difference in glycemic control.[37] In addition, we found two systematic review/meta-analyses. Yokoyama et al.[42] found that the evidence supports plant-based diets for glycemic control, but left out the follow-up Kahleova study, while Ajala et al.[43] concluded that the evidence is only suggestive of benefit.

Summary of evidence: In sum, of seven known trials[29,31,33,36,38,40,] and two-follow-up studies[34,39] on plant-based diets' effect on HbA1c, all showed an improvement from baseline. However, only two showed significant improvement compared to a control diet[36,40]. The two follow-up studies found that significant benefit had been lost[34,39] after the intervention was complete. Overall, the evidence indicates that a plant-based diet with calorie restriction may be appropriate for some people with diabetes, particularly those with a personal preference for such an eating pattern. However, the mixed findings on efficacy and the increase in triglycerides seen in some studies[33,38,40] suggest that a plant-based diet is not effective for everyone and other approaches should be considered.

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Low Carbohydrate Diet

Cited evidence. The ADA documents cite 19 studies (Table 1) in their review of low-carbohydrate diets.[45-63] Of the 13 RCT trials cited, two were inappropriately included as noted in Table 1. Of the remaining 11 RCTs, seven found a significant between-group advantage for the low-carbohydrate arm for glycemic control or insulin reduction.[45-48,61,62] Of the five that did not show a between-group glycemic advantage, three had greater reductions in medication use.[51,52,60] Two showed improvements HbA1c sustained at one year,[45,46] and two sustained benefits at two years.[48,60] Of the eight studies that reported lipids, six saw significant improvements in triglycerides, HDL or both, and none found worsening of LDL-C.[46,47,49,52,55,62] Five systematic reviews were found, of which four determined that there was evidence supporting the use of low-carbohydrate diets in patients with T2D,[54,56,57,59] whereas van Wyk did not[58]. In this review of studies from meta-analyses, van Wyk concluded that adherence may be the most significant barrier to efficacy with a low-carbohydrate approach to glycemic control.[58]

Additional evidence. We identified 22 additional studies, of which 18 were published in time for inclusion in either the 2014 Recommendations or 2018 Standards (Supplemental Table S4). Of seven new RCTs[64,65,67-70,72](not follow-up or secondary study) that reported HbA1c, all had significant decreases from baseline. Four of the studies had a significant decrease in HbA1c compared to the control diet;[64,65,69,70] the three that did not have a greater medication reduction in the low-carbohydrate arm.[67,68,72] Two non-randomized studies[77,80] and four single-arm trials found significant improvements in glycemic control.[76,78,81,82] A 44-month follow-up from a crossover trial found sustained glycemic improvements,[79] whereas another follow-up study at 24 months did not. Two systematic reviews differed in that one found no advantage with a low-carbohydrate diet,[85] and the other, more recent review and meta-analysis, recommended a low-carbohydrate diet for T2D management.[84] Three other studies and a meta-analysis, published too late for inclusion in either ADA document, are worth noting. These included a large non-randomized controlled study with a high retention rate, which found a significant and sustained decrease in HbA1c, glucose, reduction in diabetes medications, and significant weight loss in patients on a low-carbohydrate diet at one year.[75] A 24-month follow-up to an RCT (early results reported in Standards 2018), resulted in

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decreases in medication use and improved glucose stability in the low-carbohydrate arm.[72] The other study at one year found a significant decrease in HbA1c in subjects on a non-calorie-restricted, low-carbohydrate diet, compared to a calorie-restricted, low-fat arm.[64] The systematic review concluded that low-carbohydrate diets may produce clinical improvements, but called for clarification of the definition for a low-carbohydrate diet and greater efforts to improve adherence.[83]

Summary of evidence: From the studies cited by the ADA and others that we identified, we found that low-carbohydrate diets appear to be the most well-studied eating pattern for T2D. The authors of the ADA guideline documents, in their evaluation of a low-carbohydrate eating pattern, raise concerns about the quality of evidence that they did not apply to other dietary patterns. For example, regarding low-carbohydrate diets, the 2014 Recommendations state, “many of the studies were small, short duration and/or low retention rates.” However, the data show that the studies on low-carbohydrate diets were altogether larger and longer than studies on any of the other dietary patterns. Another concern raised in the 2018 Standards is that there is “not a standard definition” of low-carbohydrate diets. This issue – which essentially centers on the question of what an efficaciously low carbohydrate intake level is – is easily remedied by creating a table looking at various carbohydrate intake levels (as reported by research study participants) and benefits, as we have done (Table 2). This type of taxonomy was also used in the meta-analysis by Snorgaard 2017, which showed that the lower the actual percentage of daily calories consumed as carbohydrate (as reported by research subjects), the greater the glycemic control achieved.[57] One of the key limitations observed in most studies on low-carbohydrate diet is the discrepancy on the actual carbohydrate intake. Most participants end up taking more carbohydrate at the end of the intervention from what they were initially prescribed affecting the outcome. This is a limitation that can be seen with any dietary intervention where the prescribed diet and the diet actually consumed are often very different.

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Table 2 Reported changes in the HbA1c level in different low carbohydrate studies, grouped based on the targeted and actual reported carbohydrate intake

Carb intake level	Citation	Study design	Duration	N enrolled (% completed)	Study arm (test vs. control)	Carb intake target	Carb intake reported	HbA1c change from baseline; within-group statistical significance
Very low–carbohydrate, ketogenic (≤ 50 grams/day)	Hallberg, 2018	Non-randomized, controlled parallel arm	1 yr	262 (83%)	test (VLCK)	≤ 30g/d	not reported; adherence confirmed by blood ketones test	↓18.4% SS
	Westman, 2008	RCT	24 wks	84 (58%)	test (VLCK)	<20g/day	13%E, 49g/d	↓18.1% SS
	Boden, 2005	single-arm crossover trial	14 days	10 (100%)	test	21g/d	21g/d	↓7.4% SS
	Yancy, 2005	single-arm	16 wks	28 (75%)	test	≥20g/day. Halfway to weight loss goal, 5g/day added weekly as long as weight loss continued	33.8g/d	↓16.0% SS
	Saslow, 2017 (1)	RCT	32 weeks	25 (72%)	test (VLCK)	20-50 net carb g/d	40.9 net carb g/d	↓11.3% SS
Low-carbohydrate								

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(51- 100 GRAMS/DAY TO 30%E)								
	Yancy, 2010	RCT	48 wks	146 (84%)	test (VLCK)	<20g/d	at 48 wks: 14.6%E, 62g/d	↓6.0% SS
	Krebs, 2013	single arm	24 weeks	14 (86%)	test (very low-carb)	<20g/d	at 24 wks: 16.5%E	↓17.6% SS
	Tay, 2015	RCT	1 yr	115 (81%)	test (very low-carb)	<50g/d, 14%E	at 9-12 mos: 16.6%E	↓13.7% SS
	Saslow, 2017 (2)	RCT	1 year	34 (85%)	test (VLCK)	20-50 net carb g/d	at 1 year: 73.7 net carb g/d	↓7.9% SS
	Guldbrand, 2012	RCT	2 yr (6 mos results)	61 (100%)	test (low-carb)	20%E	at 6 mos: 25%E	↓5.3% SS
	Yamada, 2014	RCT	6 mos	24 (100%)	test (low-carb)	70-130g/d	at 6 mos: 29.8%E, 125.7g/d	↓8.6% SS
	Goday, 2016	RCT	4 mos	89 (85%)	test (VLCK)	<50g/d	32-89g/d	↓13.0% SS
	Dyson, 2007	RCT	3 mos	13 (92%)	test (low-carb)	≤ 40g/d	56.8g/day	↓5.5% unknown
	Nielsen, 2008	F-U to 6 mos n-RCT	44 mos	31 (74%)	test (low-carb)	20%E 80-90g/day	unknown	↓15.0% SS
MODERATE-CARBOHYDRATE (30-40%E)								
	Guldbrand, 2012 see above		2 yr results		test (low-carb)	20%E	at 12 mos: 31%E	0% change

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	Davis, 2009	RCT	1 year	105	test (low-carb)	20-25g/day for 2 wk induction, then 5g added weekly	at 12 mos: 33.4%E, 137g/d	0% change
	Stern, 2004	follow-up	F-U at 1 yr for 6-mos RCT	54 (63%)	test (very low-carb)	<30g/d	at 1 yr: 32.8%E, 120g/d	↓10.8% SS
	Daly, 2006	RCT	3 mos	102 (78%)	test (low-carb)	≤70g/d	at 3 mos: 33.5%E, 109.5g/d	↓6.1% SS unknown
	Sasakabe, 2011	single arm	6 ms	63 (83%)	test (low-carb)	none	at 5 mos men: 34.5%E women: 40.6%E	men ↓22.6% SS women ↓18.6% SS
	Iqbal, 2010	RCT	2 years (6 mos results)	144 (47%)	test (very low-carb)	<30g/d	at 6 mos: 35.4%E, 159.8g/d	↓6.3% SS
	Samaha, 2013	RCT	6 mos	132 (60%)	test (very low-carb)	≤30g/d	at 6 mos: 37%E	↓7.7% SS unknown
	Wolever, 2008	RCT	1 yr	162 (?)	test (low GI)	unknown	39%E	↑ 3.3%

Treatment guidelines must be based on rigorous scientific standards that are consistently applied in order to ensure that guidelines are both reliable and credible. In reviewing in detail these ADA documents on nutrition, we have found multiple reasons for concern. Not apparent in either the 2018 Standards or the 2014 Recommendations is a description of a strategy that was used to guide decisions about which studies to include. Perhaps that is the source of the issues we find concerning; for example, inclusion of studies that were not on persons with diabetes or were not clinical trials or systematic reviews of clinical trials. Additionally, the inclusion of opinion pieces that are cited as evidence raises concerns. Further, there is inconsistency, it seems, in the ADA's criteria of evidence needed to recommend an eating pattern. For example, the DASH diet is recommended citing only a single clinical trial in patients with diabetes evaluating glycemic control, while the low-carbohydrate diet is not a recommended eating pattern despite the significant evidence cited. This raises concerns about the possibility of bias. Also, the 2014 Recommendations conclude that vegetarian and low-fat vegan studies "did not consistently improve glycemic control or CVD risk factors except when energy intake was restricted, and weight was lost," yet each Standards published since has recommended plant-based as an eating pattern.

Multiple organizations have issued standards on the process for reviewing scientific evidence in order to ensure that guidelines affecting clinical care are created using the most rigorous and unbiased methods possible (Supplemental Table 5). The section of the ADA guidelines on HbA1c target guidance was recently reviewed and assessed by the American College of Physicians when this group issued new HbA1c target guidance. Using the Agree II instrument for evaluation, the American College gave a score of 3.7 out of 7 for the ADA guidelines, the second lowest of six guidelines scored. Additionally, the ADA was scored significantly lower than all other guidelines in "rigor of development." Supplemental Table 6 provides our assessment of the ADA guidelines using the National Academies of Sciences, Engineering and Medicine's *Clinical Practice We Can Trust* evaluation method, along with recommended steps for improving the overall process.

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CONCLUSION

In order to reverse the global trajectory of diabetes that we currently face, it is imperative that health organizations be willing to invest resources in creating objective guidelines based on rigorous and unbiased scientific review. A bias for maintaining the status quo despite new evidence must be overcome. At times, this may require admitting to a lack of evidence rather than issuing guidelines based on weak or incomplete evidence. Guidance from the ADA is valuable on many fronts. However, our review of the current Standards and Recommendations finds significant shortcoming regarding to scientific review methodologies which are likely to translate to suboptimal clinical care decisions for patients with T2D.

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SJH - employee of Virta Health, a for-profit company that provides remote diabetes care, and serves as an advisor for Atkins Corp.

NED - is a paid consultant for Virta Health

JK - serves as a consultant for Lexicon Pharma and Sanofi

SJA - employee of Virta Health, a for-profit company that provides remote diabetes care

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