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ANALYTIC REVIEW

Type 2 Diabetes Remission and Lifestyle Medicine: A Position Statement From the American College of Lifestyle Medicine

Abstract: Objectives. *The present review represents the position of the American College of Lifestyle Medicine on type 2 diabetes (T2D) and remission treatment.* Background. *Research now reveals that sufficiently intensive lifestyle interventions can produce remission of T2D with similar success to bariatric surgery, but with substantially fewer untoward side effects.* Methods. *A literature review was conducted to examine lifestyle modifications targeting T2D remission, with most studies using a combination of blood glucose markers and treatment history.* Results. *There were notable differences in the dosing intensity of lifestyle interventions between therapeutic interventions and subtherapeutic interventions. Studies with therapeutic dosing typically used very low energy diets (600-1100 kcal/day) with a weighted mean remission rate of 49.4%, while studies with subtherapeutic dosing typically used more moderate caloric restrictions (reducing energy intake by 500-600 kcal/day) and the weighted mean remission rate was 6.9%.* Conclusions. *Remission should be the clinical goal in T2D treatment, using properly dosed intensive lifestyle*



interventions as a primary component of medical care for T2D patients.

Keywords: lifestyle medicine; type 2 diabetes; remission; reversal; plant-based diet

Objectives

The objectives of this position paper are to (1) present the position of the American College of Lifestyle Medicine

(1) sufficiently intensive lifestyle modifications are capable of producing significant clinical improvements in patients with T2D and (2) that the optimal treatment to bring about remission (defined below) includes a whole food, plant-based (WFPB) dietary pattern coupled with moderate exercise. A WFPB diet emphasizes fruits and vegetables, legumes, and whole grains, and includes nuts and seeds while eliminating or minimizing animal foods

 . . . sufficiently intensive lifestyle modifications are capable of producing significant clinical improvements in patients with T2D. 

(ACLM) on type 2 diabetes (T2D) treatment and remission, (2) provide support for this position by reviewing the evidence base and key intervention studies on T2D remission, and (3) issue a call to action for adopting remission as the appropriate treatment goal.

The position of the ACLM, informed by current best research evidence, is that

such as red and white meat, poultry, fish, eggs, and dairy, as well as refined foods that include added sugars and oils. ACLM is in agreement with the position stated by the group who conducted the Counterpoint Study on the reversibility of T2D, “Diabetes reversal should be [the] goal in the management of Type 2 diabetes.”¹

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Furthermore, we propose that remission should always be held as the *primary* clinical goal and that lifestyle medicine interventions that produce changes leading to remission should therefore become the standard of care. There are certain logical consequences that naturally follow from this position: (1) the option for such treatment should be presented to patients in an informed consent process before other treatment offering minimal possibility for remission is prescribed and (2) reimbursement supporting this approach should be provided for such lifestyle medicine treatment.

Background

Prevalence of T2D globally was 108 million in 1980.² By 2014, the global population registered 422 million T2D cases, and prevalence is expected to rise another 50% to 642 million by 2040.³ Today in the United States, the total of diagnosed and undiagnosed cases is approximately 34.2 million, and as many as 88 million are prediabetic.⁴ The total yearly cost of diagnosed diabetes in the United States is estimated to be \$327 billion, including \$237 billion in direct medical costs and \$90 billion in decreased productivity.⁵ The highest rates of diabetes are among older, more obese patients, and patients with hypertension; while those with longer diabetes duration, and those with diabetic complications, especially chronic kidney disease, have the highest mortality rates.⁶

The current “disease management” approach for patients with T2D is primarily aimed at delaying progression of the disease rather than remission.^{7,8} In addition to the burden of disease and expense, causes for concern include the development of end-stage organ damage such as retinopathy, nephropathy and end-stage renal disease, nonalcoholic fatty liver disease, and cardiovascular disease.⁷⁻⁹ We are now seeing increased disease and mortality in younger populations with T2D.¹⁰ A shift toward treatment that can not only prevent but also reverse T2D and produce complete

remission is the single greatest need in T2D care. The field of lifestyle medicine (LM) is poised to make this contribution.

Several definitions of T2D remission have been circulated. The ACLM uses the definition published by Buse et al in 2009,¹¹ which requires blood glucose levels on par with a healthy individual without diabetes.

Remission is defined as achieving glycemia below the diabetic range in the absence of active pharmacologic (anti-hyperglycemic medications, immunosuppressive medications) or surgical (ongoing procedures such as repeated replacements of endoluminal devices) therapy . . . of at least 1 year's duration . . .

- Partial remission is subdiabetic hyperglycemia (A1c not diagnostic of diabetes [$<6.5\%$], fasting glucose 100 to 125 mg/dL)
- Complete remission is a return to “normal,” measures of glucose metabolism (A1c in the normal range [$<5.7\%$], fasting glucose <100 mg/dL)

Another leading definition of remission comes from the Association of British Clinical Diabetologists (ABCD) and the Primary Care Diabetes Society (PCDS),¹² who propose a similar but simpler and less stringent definition requiring blood glucose levels to fall below the diagnostic criteria of diabetes (what Buse et al define as “partial remission”) for a period of only 6 months. Individuals who meet the stricter definition of remission from Buse et al would therefore also meet the British definition.

A growing number of clinical experts are discussing the concept of remission as a treatment goal,¹³⁻¹⁶ inspired by the outcomes observed following weight loss,¹⁷ fasting/fasting mimicking diets,¹⁸ bariatric surgery,¹⁹ and, more recently, intensive lifestyle modifications.²⁰ Given the current upwards trend in diabetes incidence, recognizing the need for sufficiently intensive lifestyle change in diabetes treatment is essential to advance solutions that treat the cause of disease and contain the spiraling cost⁵ of diabetes management.

Methods

A literature search was performed in PubMed with no date restrictions to identify papers with search terms “diabetes” and either “remission” or “reversal” in the title through April 9, 2020. A total of $N = 914$ results from this literature search were returned, which were title-screened by a single investigator (MK) for relevance to diabetes remission in populations with T2D. A total of $n = 52$ potential papers were identified after title screening the results from this literature search. In addition, the literature search was combined with hand searching, reviewing reference lists of review papers, and prior knowledge of the authors. Following title and abstract screening, the list of papers of potential relevance were confirmed by a second investigator (JK). Full-text papers were reviewed as needed.

Key intervention studies relevant to the topic of T2D remission were selected ($n = 9$). Studies were included as key examples of either effective interventions with appropriate, therapeutic dosing levels ($n = 5$), or ineffective interventions with subtherapeutic dosing levels ($n = 4$). The distinction between therapeutic versus subtherapeutic dosing was not solely based on treatment goals but rather on whether the intervention was able to produce remission results among a substantial proportion of participants. Studies were included if they met the following minimum criteria: (1) they were intervention trials of any design conducted in humans, (2) they examined remission of T2D, (3) diabetes medication use was reported, and (4) the definition of “remission” incorporated fasting plasma glucose, hemoglobin A1c (HbA1c), and/or oral glucose tolerance test.

Studies that were conducted in animal models or were not focused on remission of T2D were excluded. Studies were not assessed for risk of bias or level of evidence.

Descriptive data were extracted by a single investigator (KC) and checked by a second investigator (MK), with

assistance from 2 additional investigators (JK and GS). The data extraction form was approved by all coauthors. Data tables were formatted through consensus-discussion and revised from the data extraction form to their final form as presented in Tables 2 and 3. If more than one paper was published on the same study, the most relevant publication to the topic of remission was selected.

Weighted mean remission rates were calculated by multiplying the remission rate for each study by the number of subjects in the study, then dividing the sum of those calculations by the sum of the number of subjects in the studies combined. A complete remission rate of zero was assumed for those studies only reporting partial remission. A partial remission rate equal to the complete remission rate was assumed for studies only reporting complete remission.

Results

Literature Review

Included interventions used a variety of lifestyle modifications to achieve T2D remission, typically involving diet and exercise. The definitions of remission varied, including using serum glucose measures alone, or in combination with other measures and being medication-free. Summary characteristics of included studies are presented in Table 1.

The 5 therapeutic studies (Table 2) ranged in sample size from 20²¹ to 298^{17,22} subjects. Designs included one cluster-randomized trial,²² one case-control pilot study with a single arm,²³ and 3 single-arm, pre-post interventions.^{21,20,24} The rates for partial remission ranged from 42%^{17,22} to 100%,²³ with a weighted mean of 49.4%. The rates for complete remission ranged from 0% to 100%.²³ Weight loss ranged from 11²⁴ to 33.7²³ lbs with a weighted mean of 19.5 lbs. The caloric content of the intervention diets ranged from 600²¹ to 1500²⁰ kcal.

The 4 subtherapeutic studies (Table 3) ranged in sample size from 8²⁵ to 5145²⁶ subjects. Two studies were randomized,^{26,27} and 2 studies used a

single-arm pre-post^{25,28} design. The rates for partial remission ranged from 13%²⁷ to 43%,²⁵ with a weighted mean of 6.9%. The rates for complete remission ranged from 0% to 10%.²⁸ Weight loss ranged from 6²⁷ to 25²⁹ lbs, with a weighted mean of 7.7 lbs. The caloric content of the intervention diets ranged from 800²⁵ to 1500²⁶ kcal in 2 studies, and stated a goal of reduction in total caloric content by 500 kcal²⁸ to 625 kcal²⁷ in 2 other studies.

Commentary on the dosing and effectiveness are included in the rightmost columns of Tables 2 and 3.

Discussion

The literature review supports the feasibility of T2D remission in diabetic patient populations using lifestyle as a primary means of treatment. Physical activity appeared to have a minor role compared to diet. While most studies increased physical activity,^{20,22,26-28} some studies achieved remission without an increased exercise protocol.^{20,24} Nevertheless, physical activity has been shown to improve insulin resistance³⁰ and beta-cell function.³¹

Mechanisms of T2D and Remission

The underlying causes of T2D have long been identified as excess weight,^{32,33} and insulin resistance.³⁴ There has been a lack of consensus on whether insulin resistance may be caused by excess weight, or whether excess weight is caused by insulin resistance.^{35,36} It has been suggested that there is bidirectional relationship.³⁷ However, one thing these 2 “causes” have in common is that they most often result from excessive caloric intake. This causes rapid insulin resistance due to increased oxidative stress, in as little as 1 to 2 days.³⁵ This occurs before weight has been gained. Ongoing intake of excess, poorly chosen calories maintains the insulin resistance.

Human physiology preserves and conserves calories, even when consumed to excess as illustrated by morbid obesity. While adipose tissue stores much of the excess calories, as

the excess accumulates it is stored in other tissues, notably in the liver, pancreas, and muscle.³⁸ In these non-adipose tissues caloric excess leads to lipotoxicity, meaning the excess fat (intracellular lipids) stored in these cells inhibits their proper functioning.³⁹ This disrupts normal glucose and insulin metabolism. Myocellular lipotoxicity inhibits glucose uptake by affecting the Glut-4 transporter.⁴⁰ This produces peripheral insulin resistance, requiring greater amounts of insulin to “push” glucose into muscle tissues. This resistance is reduced with exercise as muscle tissues consume energy and become more responsive to insulin.³⁰

Pancreatic lipotoxicity, on the other hand, inhibits beta-cell insulin production, reducing the amount of insulin available to overcome the insulin resistance in muscle and other energy-consuming tissues.⁴¹ Dramatic caloric restriction has been shown to remove triacylglycerols from the pancreas and liver in a matter of days, restoring beta-cell insulin production.²³ This occurs before significant weight loss happens, indicating it is not the excess weight but excess calories³⁵ driving insulin resistance and T2D. Over time, this also drives weight gain.

Thus, as caloric intake exceeds energy needs and overwhelms the storage capacity of adipose tissue, energy is stored in non-adipose tissues, causing lipotoxicity. This process produces weight gain as the unused energy is conserved and stored. The lipotoxicity disrupts cellular glucose and insulin metabolism, resulting in insulin resistance and beta-cell dysfunction. As this metabolic state continues and worsens, beta-cell production declines until hyperglycemia occurs. Secretagogues (which increase insulin secretion) and exogenous insulin increase insulin levels to “push” glucose into cells, sustaining the toxic metabolic state and accelerating the dysfunction. Metformin reduces peripheral insulin resistance,⁴² but this does not remove the underlying toxic etiology of excess caloric intake. Until the cause is removed, metabolic dysfunction must

Table 1.
Summary Characteristics of Intervention Studies Examining T2D Remission.

Study	Study design	Duration intensive	Duration total	Size	kcal	Controls	Weight loss (lbs)	Remission partial	Remission complete
Therapeutic studies									
Lean ^{17,22}	Randomized	4 months	2 years	298	839	Standard	19.4	42%	NR
Lim ²³	Case control	8 weeks	—	24	1150	Matched	33.7	100%	100%
Sarathi ²⁰	Pre vs post	3 months	2 years	32	1500	NA	16.3	46.9%	46.9%
Steven ²⁴	Pre vs post	8 weeks	—	30	662	NA	11.0	69%	NR
Umphonsathien ²¹	Pre vs post	10 weeks	14 weeks	20	600	NA	21.0	75%	NR
Ranges		8 weeks to 4 months	8 weeks to 2 years	20-298	600-1500		11-33.7	42% to 100%	0% to 100%
Weighted means							19.5	49.4%	
Subtherapeutic studies									
Ades ²⁸	Pre vs post	—	6 months	12	-500	NA	21.3	NR	10%
Gow ²⁵	Pre vs post	8 weeks	34 weeks	8	800	NA	14.7	43%	NR
Gregg ²⁶	Randomized	1 year	4 years	5145	1500	DSE	7.7 ^a	NR	11% to 3.5%
McInnes ²⁷	Randomized	8-16 weeks	20-28 weeks	83	-625	Standard	6.0	13%	NR
Ranges		8 weeks to 1 year	20 weeks to 4 years	8-5145	800-1500		6-21.3	10% to 43%	0% to 11%
Weighted means							7.7	6.9%	

Abbreviations: NA, not applicable; NR, not reported.

^aEstimated (actual data not reported).

Table 2.
Type 2 Diabetes Interventions With Therapeutic Dosing.

First author, publication year (ref), study design/study duration (months)/study population	Total enrolled/analyzed [F%]; M, baseline mean age (SD or SE), and mean BMI (SD or SE)	Intervention treatment	Control treatment	Remission definition	Remission rate and weight loss (kg) or change in BMI (kg/m ²)	Dosing effectiveness comments
Lean, 2018, ²² and 2019. ⁷⁷ Diabetes Remission Clinical Trial (DIRECT), cluster-randomized trial Duration: 12 months, with 24 month follow-up UK, adults 20-65 years, type 2 diabetes <6 years, BMI 27-45 kg/m ² 6% < HbA1c < 12%, weight loss <5 kg in past 6 months, and not receiving insulin. Other comorbidities were excluded If HbA1c < 6.5%, participants must be on antidiabetic medication * Intervention: baseline, and 12-month results data extracted from 2018 paper. ** 2-year follow-up results extracted from 2019 paper.	298/290 [90%]—12 months 298/272 [91.3%]—24 months Intervention N = 142 Age mean (SD) 52.9 (7.6) years 35.1 (4.5) kg/m ² Control N = 148 Age mean (SD) 55.9 (7.3) years 34.2 (4.3) kg/m ²	Evidence-based weight management program (Counterweight-Plus) with aim to reach and maintain at least 15 kg weight loss Diet replacement with low energy formula diet (825-853 kcal/day; 59% carbohydrate, 13% fat, 26% protein, 2% fiber) for 3-5 months Structured food reintroduction of 2-8 weeks (about 50% carbohydrate, 35% total fat, and 15% protein). Monthly visits for long-term weight loss maintenance Maintain usual PA during meal replacement stage; Step counters and PA strategies during food reintroduction stage, targeting up to 15 000 steps per day.	Standard care using current guidelines and standards from the National Institute of Health and Care Excellence in England and the Scottish Intercollegiate Guidelines Network in Scotland	HbA _{1c} < 6.5% after at least 2 months off all antidiabetic medications	12 months Remission Intervention 46% Control 4% Weight loss of >15 kg Intervention 24% Control 0% Mean weight loss Intervention 10 kg Control 1 kg (P < .0001 vs intervention) 24 months Remission Intervention 41% Control 3% (P < .0001 vs intervention) Weight loss of >15 kg Intervention 11% Control <1% (P = .0023 vs intervention) Mean weight loss, kg (SD) Intervention 7.6 (6.5) Control 2.3 (5.2) (P < .0001 vs intervention)	This large cluster-randomized clinical trial used intensive energy restriction (825-853 kcal/day). Partial remission (HbA1c < 6.5%) was achieved by 46% in the intervention group vs 4% of controls. The rate was 86% in intervention subjects losing > 15 kg. The study shows that sufficiently dosed, dietary lifestyle interventions can produce remission in a standard clinical practice setting.
Lim, 2011. ²³ case-control pilot single-arm intervention, Counterpoint Study Duration: 2 months UK adults age 35-65 years Cases had type 2 diabetes <4 years, HbA1c 6.5% to 9.0%, stable BMI 25-45 kg/m ² Excluded if: • Being treated with thiazolidinediones, insulin, steroids or beta-blockers • Serum creatinine > 150 mmol/L • Serum alanine transaminase level > 2.5-fold above the upper limit of the reference range • Contraindications for MRI Controls matched for weight, age, and sex. Controls had no family history of diabetes, no medication, and normal glucose metabolism confirmed by standard 75 g OGTT	24/20 [85%] Mean (SD) Intervention (Cases) N = 11 49.5 (2.5) years 33.6 (1.2) kg/m ² Control N = 9 49.7 (2.5) years 33.4 (0.9) kg/m ²	8-week intervention period with provided liquid meal replacement diet (46.4% carbohydrate, 32.5% protein, and 20.1% fat, vitamins, minerals, and trace elements [510 kcal/day] Optifast, Nestlé Nutrition, Croydon, UK), plus 3 portions of nonstarchy vegetables (total energy 600 kcal/day) and nutritional counseling. Total energy ~1150 kcal/day Encouraged to drink at least 2 liters energy-free beverages, maintain usual PA. Support via regular telephone contact.	NA—no intervention given	Normalization of beta cell function (assessed by fasting insulin secretion rate) and insulin sensitivity (assessed by suppression of hepatic glucose production by insulin infusion [P = .001])	Remission rate NR but 100% remission presumed at week 8 based on remission definition Beta-cell function: At 8 weeks in intervention group the insulin secretion rate was not significantly different from control (0.46 ± 0.07 vs 0.62 ± 0.15 nmol min ⁻¹ m ⁻² ; P = .42) Insulin sensitivity: Baseline hepatic insulin sensitivity 43 ± 4% intervention vs 68 ± 5% in control (P = .001) Week 1 produced improvement in hepatic insulin responsiveness—insulin suppression of hepatic glucose production increased to 74 ± 5% (P = .003 vs baseline) Weight loss (BMI NR) Intervention 15.3 ± 1.2 kg Control NR	This small bench study measured all relevant variables associated with T2D and insulin resistance. Dosing was intensive to produce maximum treatment effect (100% of participants normalized beta-cell function insulin sensitivity). Remission rates indicate the intervention was highly effective; comparable to bariatric surgery but without the risks of surgery.

(continue)

Table 2. (continued)

First author, publication year (ref), study design/study duration (months)/study population	Total enrolled/analyzed [F%]; N, baseline mean age (SD or SE), and mean BMI (SD or SE)	Intervention treatment	Control treatment	Remission definition	Remission rate and weight loss (kg) or change in BMI (kg/m ²)	Dosing effectiveness comments
Sarathi, 2017, ²⁰ single-arm intervention Duration: 24+ months Asian-Indian young adults newly diagnosed with type 2 diabetes; analysis divided into patients with T2D reversal at 3 months and those without reversal	32/32 [100%] Mean (SD) age at diagnosis: 24.97 (3.81) years; mean (SD) age of patients who achieved reversal: 24.83 (3.34) years; patients with no reversal: 25.37 (2.82) years	Daily calorie intake of 1500 kcal (60% as carbohydrates, 15% as proteins, and 25% as fat) and brisk walking for 1 h every day Subjects with HbA _{1c} ≥9.0% were started on metformin 500-2000 mg; subjects with comorbid conditions requiring early glycemic control were started on insulin followed by oral antidiabetic agents (metformin ± DPP4 inhibitors)	NA	At 3 months, complete remission = normalization of fasting plasma glucose (<100 mg/dL At 1 year or later, complete remission = normal fasting plasma glucose of <100 mg/dL and HbA _{1c} of <-5.7%	Reversal/remission At 3 months: 53.1% At 1 year: 50% At 2 years: 46.9% Weight loss Reversal group: Mean (SD) change in weight 3 months 7.41 (2.1) kg No reversal group: Mean (SD) change in weight 3 months 4.25 (1.16) kg	This small intervention study used modest caloric restriction (total 1500 kcal/day) with moderate exercise (walking 1 h/day) in young adults with newly diagnosed T2D. Complete remission was achieved by 53% at 3 months, and by ~50% at 2 years. Adherence was not reported but weight loss at 3 months was almost twice in those achieving complete remission compared to those without.
Steven, 2015, ²⁴ single-arm intervention Trial of T2D following Counterpoint Study, participants analyzed comparing diagnosis of short duration (<4 years) or long duration (>8 years) Duration: 8 weeks UK adults age 25-80 years, BMI 27-45 kg/m ² , type 2 diabetes treated by diet, metformin, sulphonylureas, dipeptidyl peptidase-4 inhibitors and/or insulin Excluded if: • Recent weight loss >5 kg • Txt w/ thiazolidinediones, GLP-1 agonists, steroids, or atypical antipsychotics • HbA1c >9.5% • Serum creatinine >150 µmol/L • Alcohol >3 units/day (women) or >4 units/day (men)	30/29 [97%] Mean (SE) Short duration N = 15 52.1 (2.6) years 34.2 (0.8) kg/m ² Long duration N = 14 61.6 (2.0) years 34.3 (1.2) kg/m ²	Hypocaloric diet using meal replacement liquid diet formula (43% carbohydrate, 34% protein and 19.5% fat; vitamins, minerals kcal/day); Onifast; Nestle Nutrition, Croydon, UK), plus consumption of up to 240 g of nonstarchy vegetables per day (total energy (624-700 kcal). Encouraged to drink at least 2 liters energy-free beverages, maintain usual PA. Support via regular telephone contact, e-mail, text, or face-to-face contact. All medications discontinued at the start of the study.	NA	Remission not explicitly defined Study goal was to assess the proportion of short- and long-duration type 2 diabetics who achieved non-diabetic FPG levels (<126 mg/dL) The proportion of participants achieving nondiabetic HbA1c levels was also measured (<6.5%)	Short duration 87% achieved nondiabetic FPG Mean (SE) 5.8 (0.2 mmol/L) Long duration 50% achieved nondiabetic FPG FPG mean (SE) 6.2 (0.7 mmol/L) Duration 8-12 years Duration ≥12 years 10.6 (1.7 mmol/L) Change in BMI Short duration Baseline: 34.1 (0.8) Week 8: 29.1 (0.9) P < .001 Long duration Baseline: 34.3 (1.2) Week 8: 29.4 (1.1) P = .001	This intervention trial achieved partial remission in 87% in those with T2D <4 years and in 50% of those with T2D >8 years
Umphonsathien, 2019, ²¹ single-arm intervention study Duration: 3 phases 2-week run-in 8-week caloric restriction 4-week caloric transition Thai adults (age 20-60) with obesity (BMI of 25-30 kg/m ²) and T2D for <10 years	20/19 [95%] 48 (1.7) years BMI mean (SE) 27.7 (0.8) kg/m ²	Very low calorie diet (VLCD) of 600 kcal/day for 2 weeks during run-in period and for 8 weeks during study period followed by a gradual increase in calories during 4-week transition period (800 kcal/day on week 9, 1000 kcal/day on week 10, 1200 kcal/day on week 11, 1500 kcal/day on week 12)	NA	Hyperglycemia not diagnostic of DM (FPG level <126 mg/dL and HbA1c <6.5%) in the absence of active pharmacologic therapy for DM lowering medication(s)	Remission 8 weeks 79% (15/19 subjects) intention to treat analysis Remission rate of 75% at both 8 and 12 weeks Weight loss Mean (SEM) Over 14 weeks 9.5 (1.8) kg	This small cohort study used a VLCD (total 600 kcal/day) in subjects with T2D <10 years, followed by a gradual return to a 1500 kcal/day diet. Partial remission was achieved by 75% of subjects. Rates of complete remission were not reported but must have been achieved by a sizeable proportion. This study illustrates that more intensive dosing achieves greater remission.

Abbreviations: BMI, body mass index; MRI, magnetic resonance imaging; OGTT, oral glucose tolerance test; NA, not applicable; T2D, type 2 diabetes; FPG, fasting plasma glucose.

Table 3.
Type 2 Diabetes Interventions With Subtherapeutic Dosing.

First author, publication year (ref), study design/study duration (months)/study population	Total enrolled/analyzed [%], N, baseline mean age (SD), and BMI (SD)	Intervention treatment	Control treatment	Remission definition	Remission rate and weight loss (kg) or change in BMI (kg/m ²)	Dosing effectiveness comments
Ages, 2015. ²⁸ Single-arm intervention study Duration: 6 months Overweight/obese (BMI 35.8 ± 4.3 kg/m ²), sedentary, and unfit (peak VO ₂ 20.7 ± 4.7 mL/kg/min) and recently (<1 year) diagnosed with type 2 diabetes Exclusions: Taking hypoglycemic medication	1210 (83%) 62 (6) years 35.8 (4.3) kg/m ²	Behavioral weight loss counseling (24 weekly group counseling sessions coordinated by a RD and focused on self-monitoring and developing an action plan for diet and physical activity), daily caloric goal of 500 kcal less than predicted maintenance calories, supervised exercise (nearly daily sessions of "high-calorie expenditure exercise" with 1-3, 45-60 minute sessions/week of supervised on-site exercise and home walking on other days for a total of 5-6 days per week of exercise [intensity set at 50% to 60% peak VO ₂])	NA	Complete remission is an HbA _{1c} level <5.7%	Complete remission rate = 10% (1/10 participants) Average weight loss: 9.7 (5.2) kg or 9%	This small study used a subtherapeutic dose of lifestyle interventions with exercise and an energy deficit diet of ~500 kcal/day. Though fitness improved significantly, results indicate that exercise did not compensate for the subtherapeutic dietary intervention.
Gow, 2017. ²⁵ Single-arm intervention Duration: 8 weeks of very-low-energy-diet (VLED) 34 weeks hypocaloric diet Patients divided into adherers (≥5% body weight loss during the 8-week VLED) and non-adherers Australasian and New Zealand youth, age <18 years, obese, type 2 diabetes	8/8 (100%) for 8-week VLED 8/5 (63%) for 34 weeks hypocaloric diet Age median (range) 14.4 (7.5-16.8) years Weight mean (SE) 86.2 (10.2) kg	Weeks 0-8 VLED 800 kcal/day <40% carbohydrate 40-55% protein <20% fat Weeks 9-12 Transition to reduced-energy diet, weaning away from meal replacements Weeks 13-24 Hypocaloric diet (45% to 55% moderate glycemic index and minimal refined carbohydrate, 15% to 25% protein and ~30% fat where <10% saturated) Support given throughout via regular telephone/text message contact	NA	HbA _{1c} levels <6.5%, fasting plasma glucose <7.0 mmol/L or 2-hour post-glucose load plasma glucose <11.1 mmol/L	Remission All participants 50% Adherers only After 34 weeks = 80% Weight loss All participants Mean (SD) weight loss after 8-week VLED = 4.1 (4.0) kg or 5.0 (4.3) % body weight Adherers Median weight loss after 8-week VLED = 7.5%, median (range) weight loss after 34 weeks = 6.7 (3.4-13.2) kg, or 12 (3.7-14.3) % body weight Non-adherers Median weight loss after 8-week VLED = 0.5%, after 34 weeks NA (all non-adherers discontinued participation)	This small study illustrates the potential of intensive lifestyle changes to produce remission when properly dosed. It also illustrates the ineffectiveness of insufficiently dosing lifestyle changes in the non-adherent subjects.
Gregg, 2012. ²⁹ ancillary observational analysis of LookAHEAD randomized controlled trial 48 months US adults, 45-76 years, BMI ≥25 kg/m ² , type 2 diabetes Excluded if: • HbA _{1c} >11% • BP >160 mm Hg systolic or >100 mm Hg diastolic • TAG >600 mg/dL • Unable to perform a maximal graded exercise test • Unable to complete 2 weeks of diet and activity self-monitoring	5145/4503 (88%) Intervention N = 2241 58.6 (6.7) years 35.8 (5.9) kg/m ² Control N = 2262 59.1 (6.9) years 35.9 (5.7) kg/m ²	"Intensive lifestyle intervention" (LI) First 6 months: weekly group and individual Second 6 months: 3 sessions per month Years 2-4: 2 sessions per month and regular refresher group series Goals: Reduce total caloric intake to 1200 to 1800 kcal/d through physical activity to 175 min/week Liquid meal replacements provided	Diabetes support and education (DSE) 3 group sessions per year on diet, physical activity and social support	Full normalization of glucose (fasting) plasma glucose level <100 mg/dL and HbA _{1c} <5.7% with no anti-hyperglycemic medication	2-Year Intervention: 9.2% (95% CI: 7.9% to 10.4%) Control: 1.7% (95% CI: 1.2% to 2.3%; P .001) 3-Year Intervention: 6.4% (95% CI: 5.7% to 7.4%) Control: 1.5% (95% CI: 0.8% to 1.7%; P .NR) 4-Year Intervention: 3.5% (95% CI: 2.7% to 4.3%) Control: 0.5% (95% CI: 0.2% to 0.8%; P = .02) Weight loss: ~3.5%	The LookAHEAD study used what they called "intensive lifestyle interventions" (LI), which consisted of a modest energy restriction (1200-1800 kcal/day) with exercise. The modest weight loss and minimal remission reveals the lifestyle changes were insufficiently dosed. Compare these results to outcomes of studies in the therapeutic table above (DIRECT, Counterpoint, etc. The LookAHEAD trial illustrates why lifestyle change has been considered ineffective—underdosed LM interventions are ineffective.
McInnes, 2017. ²⁷ 3-arm parallel randomized controlled trial 8 or 16 weeks intervention plus follow-up until 52 weeks (12 months total) Patients of Diabetes Care and Research Program at Hamilton Health Sciences; 30-80 years, T2D for up to 3 years, BMI ≥23 kg/m ²	8383 (100%) 8-Week intervention N = 28 57.1 (10.3) years 34.7 (7.0) kg/m ² 16-Week intervention N = 27 55.1 (9.2) years 33.3 (6.5) kg/m ² Control N = 28 58.2 (11.1) years 31.6 (4.4) kg/m ²	In-person and phone counseling reduction of daily kcal by 500-750 Treatment with metformin, acarbose, and insulin glargine Moderate physical activity >150 min/day	Standard diabetes care	Complete remission FPG <6.1 mmol/L and 2-hour plasma glucose <7.8 mmol/L on an OGTT Or HbA _{1c} <6.0% and no chronic diabetes drugs (% participants)	8-Week group Using OGTT criteria: at 20 weeks post-randomization, complete remission = 7.1% HbA _{1c} criteria: 20 weeks post-randomization, complete remission = 10.7% 16-Week group OGTT criteria: 20 weeks post-randomization, complete remission = 14.8%; 28 weeks post-randomization, complete remission = 7.4%; HbA _{1c} criteria: 28 weeks post-randomization, complete remission = 14.8% Control group OGTT criteria: 28 weeks post-randomization, complete remission = 3.6%; HbA _{1c} criteria: at 28 weeks post-randomization, complete remission = 7.1% Weight loss 20-week post-randomization weight loss mean % (SD): 8-week: 3.1 (3.4) 16-week: 5.1 (3.3) Control: 1.4 (2.4)	This RCT used a moderately hypocaloric diet (reduced by 500-750 kcal/day) with moderate physical activity (>150 min/day). This moderate dosing achieved moderate complete remission rates of ~7% to ~15%. Exercise levels were not measured, but BMI changes indicate moderate weight loss occurred. This study shows that exercise cannot compensate for an insufficient dietary energy deficit.

Abbreviations: BMI, body mass index; NA, not applicable; BP, blood pressure; CI, confidence interval; T2D, type 2 diabetes; FPG, fasting plasma glucose; OGTT, oral glucose tolerance test; RCT, randomized controlled trial.

continue. The dysfunction is in reality a normal physiologic response to the toxic state induced by excess calories.

Some of the newer diabetes medications are designed to cause the kidneys to spill glucose into the urine as a way to lower serum glucose.⁴³

Normally, the kidneys strictly conserve glucose as the body's main energy source. When glucose spills into the urine it fuels bacterial growth, which can result in a urinary tract infection, requiring treatment to avoid systemic infection and sepsis. It is therefore common for individuals using these medications to be prescribed antibiotics on an ongoing basis to control the urinary tract infections.^{8,43}

In sum, these treatment complications are the direct result of an attempt to eliminate the excess glucose from overconsumption of calories.

Importance of Dosing

The importance of appropriate dosing in the context of lifestyle modification can hardly be overstated. Dosing is of prime therapeutic importance in a pharmaceutical context; with LM it is no different. Simple aspirin provides an excellent illustration—treatment for headache requires aspirin dosing of 325 to 650 mg once or twice a day. This outcome cannot be achieved using a dose of 81 mg aspirin daily, the dosing typically prescribed as an antithrombotic agent.

The same dosing principles apply to LM; the lifestyle modifications required to produce T2D remission are significantly more intensive than those sufficient to prevent T2D. Clinicians whose patients achieve remission do so by making sufficiently dosed lifestyle changes (eg, diet, exercise, etc). Remission has not been reported with inadequately dosed lifestyle changes, such as eating more salad, or simply reducing meat consumption. Research now shows that remission is achievable for a majority of short duration (<8 years) T2D patients, and many with longer duration, with sufficiently intense LM interventions.^{22,23} Most failures are due to inadequate dosing of LM, and not

to any inherent deficiency of LM as treatment. Patients find intensive LM treatment acceptable and desirable when treatment produces remission.¹ A personal demonstration of remission can reset the lifestyle goals patients set for themselves.

At the same time, degree of dosing is also influenced by patient willingness to change⁴⁴ and the inherent challenges in making healthy changes⁴⁵ without adequate support and guidance. Adherence to conventional diet and lifestyle guidelines for diabetes management has been identified as problematic for T2D patients specifically.⁴⁶ Key barriers to adherence include lack of communication and support from health care providers, as well as inadequate education.⁴⁷ We argue that this underscores the importance of working with specialists trained in LM⁴⁸ to provide the education, support, and modeling necessary to successfully and realistically achieve a sufficiently strong intervention dose and accomplish the goal of remission.

Therapeutic Dosing

Research shows that sufficiently intensive dosing of lifestyle interventions will induce remission in half or more of all subjects with T2D. Studies also reveal that not all lifestyle interventions produce remission, and that remission rates are lower for longer-duration T2D. Adherence and other individual factors also affect remission rates. The highest remission rates are similar to those with bariatric surgery.^{22-24,49}

The case-control study by Lim et al from 2011 provides a strong example of appropriate, therapeutic dosing.²³ This study achieved immediate remission (1-4 weeks) with a very intensive LM intervention, prior to significant weight loss. The Counterbalance study by Steven et al from 2015 is another example of therapeutic dosing.²⁴ These researchers chose to use liquid meal replacements with good effect. Rehackova et al⁵⁰ conducted semistructured interviews of participants before and after completion of the 8-week Counterbalance study and found high acceptability for the VLED

(very low energy diet) meal replacement. Steven et al published self-reported remission in subjects inspired by the Lim paper to make intensive lifestyle changes on their own,¹ indicating the presence not only of high acceptance but also high motivation for diets that induce remission. Few people are willing to make dramatic changes in behavior unless they can perceive meaningful benefit.

Not all attempts at T2D remission are equally successful. Not all lifestyle interventions are of equal strength or intensity. The LookAHEAD study compared standard DSE (sDSE) to what researchers called an "intensive lifestyle intervention" (ILI), achieving a remission rate ~4 to 6 times higher with ILI than with the sDSE.²⁶ This sounds excellent until we learn that the sDSE rate was ~2% while the ILI rate was ~6% to 12%. When compared to adequately dosed LM such as that used in the DiRECT and Counterpoint trials, which achieved remission rates of 46% to 86%, and the 6% to 12% is subtherapeutic.

Similarly, in the pilot study by Ades et al,²⁸ partial remission was achieved in 70% of completers (7 of 10) but complete remission in only 10% (1 of 10). The subjects had recently been diagnosed with T2D (mean 93 days) and would be expected to achieve remission more readily than those with long-duration disease. The dosing was insufficient to produce the remission that more intensive dosing achieves. The diet was only 500 kcal less than required for weight maintenance. This dosing is more suited for prevention than remission. While more effective than the LookAHEAD trial, compared the therapeutic dosing rates of 46% to 86% in the DiRECT and Counterpoint trials, it is subtherapeutic.

Plant-Based Diets Versus Meal Replacements

Other T2D and weight loss researchers have used unprocessed plant-based diets with good effects,⁵¹⁻⁵³ indicating that liquid meal replacements may be unnecessary to achieve the very low energy diets

needed for remission. A study of 5 diets by Turner-McGrievy et al from 2015 found a totally plant-based diet (vegan) was more effective in reducing energy intake than other diets tested, leading to significant weight loss.⁵⁴ The fasting mimicking diet studied by Cheng et al found a periodic fast restored beta-cell function and normoglycemia in T1D and T2D mouse models, with similar in vitro effects in human pancreatic tissue.⁵⁵ Intermittent fasting has been found effective in reducing hyperglycemia and stimulating beta-cell neogenesis.^{18,56}

Very low energy diets and fasting, whether using liquid meal replacements, fasting mimicking diet, or simply intermittent fasting, can be quite effective. This is consistent with other evidence indicating that reduction or avoidance of unhealthy foods may yield a greater benefit than inclusion of healthier foods. Schwingshackl et al found consumption of risk-decreasing foods (whole grains, dairy, fruits, and vegetables) resulted in a 42% risk reduction of T2D, and consumption of risk-increasing foods (red and processed meats, sugar-sweetened beverages, and eggs) was associated with a threefold increased risk, compared to nonconsumption.⁵⁷

Current Best Evidence and ACLM's Position Statement on T2D

The numerous studies in Table 2 show that sufficiently intensive lifestyle interventions successfully produce remission of T2D and do so with a success rate comparable to other modalities, including bariatric surgery. This fact has not been recognized and has not appropriately informed or shaped the present approach to lifestyle interventions in the treatment and management of T2D. It is inconsistent with the evidence to favor higher risk, invasive treatments over lifestyle change. It is ACLM's position that this perspective on lifestyle interventions needs to change and that LM should be a primary component of every patient's treatment plan for T2D.

The studies in Table 3 demonstrate that inadequately dosed lifestyle interventions do not successfully produce remission of T2D. The present diminution of lifestyle interventions in the treatment and management of T2D is undoubtedly due in part to the failure to distinguish between therapeutically dosed interventions and subtherapeutically dosed interventions. For example, the LookAHEAD study concluded from their subtherapeutic "intensive lifestyle interventions" that lifestyle change was not sufficiently effective to be a viable alternative to bariatric surgery.²⁶ This is actually an incorrect conclusion because it was based on what appears to be a subtherapeutic intervention. Other investigators who have produced remission have arrived at a different conclusion (Table 2).

Lifestyle recommendations have not historically focused on the remission of T2D, rather focusing on glycemic improvements and disease management. Several organizations, including the American Association of Clinical Endocrinologists and the American College of Endocrinology,⁵⁸ acknowledge the benefit of a plant-based diet as the optimal nutrition plan for the management of T2D.⁵⁸ In fact, the International Diabetes Federation³ plainly states that lifestyle behavior, including poor diet, is the most influential factor in the development of T2D.

In 2019, the ABCD and the PCDS published a position statement¹² on T2D remission stating that effective methods of diabetes remission included either (1) bariatric surgery or (2) a short-term dramatic caloric reduction with total dietary replacement followed by a stepped food re-introduction. Overall, there is movement in the professional medical community toward emphasizing lifestyle modifications for T2D management, though an emphasis on remission as a goal is still emerging.

The Historical Context

Although the concept of using diet to achieve remission seems new in the context of conventional treatment, it is not a new idea. Over the course of the

20th century, diet recommendations for diabetes prevention and management varied widely,⁵⁹ alternately supporting either low-carbohydrate/high-protein^{60,61} or high-carbohydrate⁶²⁻⁶⁵ eating patterns. However, instead of remission as a goal, research typically focused on glycemic improvement and disease management.^{8,66,67}

During that time, the use of medication emerged as the primary means of treatment.⁸ The discovery of insulin in 1921 was hailed as a breakthrough therapy for severe diabetes,⁶⁸ later known as type 1 diabetes. While this discovery of insulin was life-saving for patients with type 1 diabetes, it also became the standard of care for patients with type 2 diabetes. This diverted attention from the approach of seeking to reverse the condition by addressing the underlying causes. Unfortunately, the medication-oriented approach has progressed to the point that some practitioners now advocate for starting insulin immediately after diagnosis.⁶⁹ This approach may prolong beta-cell function but does not lead to remission.

Thus, a gap developed in lifestyle research and treatment, causing a lack of results around clinically significant, enduring T2D remission. Because of these failures, more dramatic interventions were sought. Bariatric surgery, despite the expense and risk of complications, started as a treatment for weight loss circa 1987⁷⁰ and became commonplace as a treatment for T2D by 2010.⁷¹ While the 30-day mortality is between 0.1% and 1.1% for bariatric surgery, the risk of developing acute and long-term complications is high (17%).⁷² The list of possible complications from bariatric surgery is wide-ranging including anemia, reflux esophagitis, marginal ulcer, nutritional deficiencies, gastrointestinal bleeding, intraabdominal abscess, intraperitoneal bleeding or minor bleeding, urinary tract infection, and wound infection, while the rate of reoperation after surgery is 7%.

A pivotal finding from bariatric surgery for morbid obesity was that it could produce T2D remission, something that had previously been considered

impossible, or at least impractical.⁸ While the search continues for a complete understanding of how bariatric surgery rapidly reverses T2D, some very informative research reveals that these results may not depend on the surgery itself.^{49,73} Lingway et al evaluated the contribution of caloric restriction versus surgically induced changes in glucose homeostasis in the immediate postoperative period among N = 10 patients in a prospective, 2-period study in which patients served as their own controls.⁴⁹ The study periods lasted for 10 days of inpatient stay, and periods were separated by a minimum of 6 weeks of a wash-out period. While no significant improvements were observed in the days immediately following the surgery, the presurgery diet intervention period produced a significant improvement in fasting glucose, maximum poststimulation glucose, and glucose area under the curve (AUC) during a mixed-meal challenge test.⁴⁹ These results support reduced calorie ingestion as the causal mechanism initiating marked improvement in glycemic control observed after Roux-en-Y gastric bypass surgery. Studies like the Counterpoint²³ and DiRECT²² trials reveal that sufficiently intense caloric restriction can indeed induce remission in a majority of T2D cases in a matter of weeks.

Glycemic Index and Blood Glucose

One view of dietary control of blood sugar revolves around glycemic index;⁷⁴ thus, the topic requires clarification in the context of diabetes remission versus management. Glycemic index (GI) calibrates the postprandial effect a food or meal has on serum glucose levels (SG) compared to ingestion of 70 g of glucose.⁷⁵ High GI values indicate the food produces a relatively greater rise in SG, whereas low glycemic index values indicate the food produces a relatively smaller rise in SG. In general, simple sugars and highly processed carbohydrate foods have relatively higher GI values, while complex and unprocessed carbohydrates and

non-carbohydrate foods (protein, fat) have relatively lower GI values.

Not all low GI foods are equivalent in their effects on metabolism, insulin resistance, and T2D, and remission is not directly related to GI.⁷⁶ Remission depends on reversing insulin resistance and restoring insulin sensitivity.²³ Thus, Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) is a better measure of the effect a food has on insulin resistance and T2D remission than GI.⁷⁷

Remission requires an energy deficit to remove liver and pancreatic triacylglycerols and stop their lipotoxic effects.²³ Thus, consuming low GI foods alone cannot produce remission without an energy deficit. Some low GI dietary patterns that help maintain a low SG do not reverse insulin resistance and do not produce T2D remission. One such pattern is the so-called “ketogenic diet,” which emphasizes a low-carbohydrate, high-fat, and high-protein eating pattern.⁷⁸

A VLED produces ketosis, but does it with an energy deficit, whereas the ketogenic diet does it by forcing the body to metabolize fats instead of carbohydrates. The diet is not energy deficient and does not reverse liver and pancreatic triacylglycerols; thus, it helps control SG but not insulin resistance.^{78,79} Ketogenic diets only appear to eliminate T2D by consistently failing to challenge insulin receptivity rather than by improving or restoring it.

Low-Carbohydrate Diets

The present swing toward a high-protein, low-carbohydrate dietary pattern for improving hyperglycemia is problematic. As summarized by Uusitupa and Schwab in their editorial on diet and T2D,⁸⁰

... there are no real long-term intervention trials on high protein diets in people with diabetes.⁸¹ ... the safety of high protein diets has been documented for one year only.⁸¹ ... the quality or quantity of dietary protein does not seem to play any role in the pathogenesis of type 1 diabetes, whereas regarding type 2 diabetes,

higher intakes of red meat and processed meat products have been consistently associated with the increased risk of type 2 diabetes⁸² and other chronic non-communicable diseases.⁸³ This should arouse concern when considering any dietary guidelines.

Long-term prevention trials of T2D have applied diets emphasizing healthy dietary patterns with typical protein intake.⁸⁴ The primary goal of the prevention of T2D is permanent weight reduction that can be achieved by healthy dietary patterns and increased physical activity.

Whole Food, Plant-Based Diets

Importantly, control of SG can also be accomplished, without negative side effects from medication, by reducing consumption of excess calories. This can be done in 1 of 2 ways: either by reducing the volume of food (holding energy density constant) or by reducing the energy density (holding the volume of food constant).⁸⁵ In order of effect size, the 3 factors of decreasing fat, increasing fruits and vegetables, and increasing water content have been shown to decrease caloric content in ad libitum eating conditions.⁸⁶ Consumption of food with lower energy density has been found to produce satiety without feelings of hunger or deprivation,⁸⁵ and portion size, independent of greater energy density, has been shown to affect satiety.⁸⁷ The dietary pattern that, when followed, offers the greatest reduction in fat content and the greatest increase in fruits and vegetables and water content is a WFPB diet.^{88,89} In observational studies this dietary pattern largely overlaps with a vegan diet (eliminating all animal products) and is associated with lower BMI and prevalence of T2D.^{90,91} This is also the diet which the authors use with the greatest success and which the surveyed ACLM member practitioners report as being most important in achieving T2D remission outcomes, when the dietary change represents an appropriately intensive dose.

Summary

Adequate research exists demonstrating that T2D remission is achievable without pharmacological interventions or surgery. The best evidence indicates that a substantial energy deficit is necessary until an adequate reduction in intracellular hepatic and pancreatic fat content is achieved to induce insulin sensitivity and glucose control. The wide variability in results among the interventions discussed here highlight the importance of appropriate dosing in lifestyle interventions, just as with other types of medical treatment.

The dietary intervention used by the authors indicates that a therapeutically dosed WFPB is the preferred intervention. This is consistent with internal ACLM survey results (as-yet unpublished data) that reveal that a large proportion of ACLM members are using diet (predominantly a WFPB diet) as the primary modality in treating and managing T2D, and that the majority have seen improvements in T2D including reduced need for medications and improved glycemia. While these data do not quantitatively capture remission outcomes, it shows support for and need of evidence-based lifestyle interventions to treat and reverse T2D, the conclusion of this position statement. A WFPB diet has multiple benefits of minimizing harmful foods, emphasizing healthy foods, reducing energy density through lower levels of fat and higher amounts of fruits, vegetables, and water. It also facilitates weight loss without feelings of deprivation or hunger, and seems well-tolerated by patients.⁹²

Regardless of the exact dietary method used to restore beta-cell function and insulin sensitivity, we recommend that T2D remission by intensive lifestyle change be the primary modality for T2D care. Published research reveals that sufficiently intensive lifestyle interventions consistently produce partial or complete remission in a significant proportion of patients. We also recommend that existing pharmaceutical therapies not be abandoned prematurely, but continue to be utilized to achieve and maintain optimal blood sugar

control, with the goal of reducing and eliminating these measures as soon as possible, as the recommended lifestyle diet and exercise modalities are applied by the patient and weight loss and restoration of normal endogenous insulin levels are restored. As more experts in the field support a nonpharmacologic approach to T2D treatment,¹⁶ rigorous research to quantify the effects of a WFPB diet as compared to other dietary interventions such as liquid meal replacements or severe caloric restriction is needed.

Limitations

There are inherent limitations present in this review. The lifestyle intervention studies of T2D remission are few in number with wide variability of design as well as being generally limited to short-term outcomes. A majority of the therapeutic studies examined would not meet the definition of remission put forth by Buse et al,¹¹ though there is a lack of consensus on duration needed to assess remission among clinicians and researchers.¹² Most studies of remission have examined T2D of short duration, and success rates are higher the earlier treatment is initiated after diagnosis. This is not a systematic review; the list of studies (Tables 1-3) is not exhaustive but rather chosen to be representative of the position statement put forth.

Conclusion

As incidence and prevalence of T2D continue to rise, the current best evidence from multiple intervention studies supports that remission achieved with intensive lifestyle modifications should become the preferred treatment and standard of care. To achieve remission, appropriate, therapeutic dosing of lifestyle modifications is necessary, including a hypocaloric diet. Future research should focus on high-quality intervention trials to further quantify the potential of different lifestyle modifications, including consumption of a low-fat, WFPB diet to achieve remission of T2D in comparison to

standard pharmacologic treatment and surgical interventions.

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Ethical Approval

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Informed Consent

Not applicable, because this article does not contain any studies with human or animal subjects.

Trial Registration

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