Supplementary material: PICO, Keywords, Synonyms and Search String for Systematic Electronic Database Search

Supplementary Table 1 Table of PICO

Population	This review will focus on adults with type-2 diabetes mellitus. Studies reporting on adult T2DM patients aged more than 18 years old will be included. Intervention including mixed population age will be included only if the data can be separated. There will be no restriction on the severity of T2DM of subjects in the study.
Intervention	Any intervention or program utilizing self-administered meal replacements will be considered. A meal replacement is defined as prepackaged food products, drinks, or meals that are designed to replace one or more meals and provide a defined amount of energy.
Comparator	No comparator is required for this review.
Outcome	Any studies that report the outcome related to the health status of the T2DM subject, including glycemic control, weight reduction, or side effects.

Supplementary Table 2 List of keywords and synonyms generated as search terms

Meal Replacement	**Type-2 Diabetes Mellitus**	**Glycaemic control**	**Weight reduction**	**Risks**
Food Substitute	Diabetic	HbA1c	Weight Loss	Side effect
Alternative Serving	Diabetes	Random Blood Sugar	Weight reduction	Danger
Diet Alternative	Non-insulin dependent Diabetes Mellitus	Glucose	Decrease in body weight	Hazardous
Alternative Nutrition	Diabetes Mellitus-onset	Fasting blood sugar	Body Weight Changes	Adverse effect
Diet Replacement	Type-II Diabetes Mellitus	2-Hour Post-Prandial Blood Glucose	BMI reduction	Bad
Diet plan Exchange		Glucose tolerance	Fatness	Negative effect
Replacement Drink			Adiposity	Harmful
Alternate nutrition				Detrimental
Oral nourishing supplement				Antagonistic
Medicinal food				Unsafe

Supplementary Table 3 List of search strings

Search string 1:	"Meal Replacement*" OR "Food Substitute*" OR "Alternative Serving*" OR "Diet Alternative*" OR "Alternative Nutrition" OR "Diet Replacement*" OR "Diet plan Exchange" OR "Replacement Drink*" OR "Alternate nutrition" OR "Oral nourishing supplement*" OR "Medicinal food" AND "Type-2 Diabetes Mellitus" OR Diabetic OR Diabetes OR "Non-insulin dependent Diabetes Mellitus" OR "Diabetes Mellitus-onset" OR "Type-II Diabetes Mellitus"
Search string 2:	"Meal Replacement*" OR "Food Substitute*" OR "Alternative Serving*" OR "Diet Alternative" OR "Alternative Nutrition" OR "Diet Replacement*" OR "Diet plan Exchange" OR "Replacement Drink*" OR "Alternate nutrition" OR "Oral nourishing supplement*" OR "Medicinal food" AND "Type-2 Diabetes Mellitus" OR Diabetic OR Diabetes OR "Non-insulin dependent Diabetes Mellitus" OR "Diabetes Mellitus-onset" OR "Type-II Diabetes Mellitus" AND "Glycaemic control" OR HbA1c OR "Random Blood Sugar" OR Glucose OR "Fasting blood sugar" OR

	"2-Hour Post-Prandial Blood Glucose" OR "Glucose tolerance"
Search string 3:	"Meal Replacement*" OR "Food Substitute*" OR "Alternative Serving*" OR "Diet Alternative" OR "Alternative Nutrition" OR "Diet Replacement*" OR "Diet plan Exchange" OR "Replacement Drink*" OR "Alternate nutrition" OR "Oral nourishing supplement*" OR "Medicinal food" AND "Type-2 Diabetes Mellitus" OR Diabetic OR Diabetes OR "Non-insulin dependent Diabetes Mellitus" OR "Diabetes Mellitus-onset" OR "Type-II Diabetes Mellitus" AND "Weight reduction" OR "Weight Loss" OR "Weight reduction" OR "Decrease in body weight" OR "Body Weight Change*"
Search string 4:	"Meal Replacement*" OR "Food Substitute*" OR "Alternative Serving*" OR "Diet Alternative" OR "Alternative Nutrition" OR "Diet Replacement*" OR "Diet plan Exchange" OR "Replacement Drink*" OR "Alternate nutrition" OR "Oral nourishing supplement*" OR "Medicinal food" AND "Type-2 Diabetes Mellitus" OR Diabetic OR Diabetes OR "Non-insulin dependent Diabetes Mellitus" OR "Diabetes

	Mellitus-onset" OR "Type-II Diabetes Mellitus" AND "Risk*" OR "Side effect" OR "Dangerous" OR "Hazardous" OR "Adverse effect*" OR "Bad" OR "Negative effect*" OR "Harmful" OR "Detrimental" OR "Antagonistic" OR "Unsafe"

Supplementary Table 4 Inclusion/exclusion criteria for study selection

Inclusion criteria	Exclusion criteria
Studies ranging from January 2000 to January 2024 related to meal replacement with T2DM-affected patients aged 18 and above (adult and elderly).	Studies that are not available in English and Malay language Studies with type-1 diabetes mellitus patients Studies with pregnant women Studies which are not human studies Studies which meal replacements that are not self-administered

Supplementary Table 5 Types, composition, dosage, and duration of meal replacement intervention for T2DM

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
Low Calorie/Energy MR (n=46)								
Rothberg et al. [1]	USA	Observational study	Clinical	66	Total Meal Replacement with HMR products (HMR®, Boston, MA) in the form of chocolate or vanilla shake or chicken soup	TDR 160-170 kcal per packet 800 kcal per day >160 kg additional 160-170 kcal/day per 23 kg	/	12 weeks
Tatti et al. [2]	Italy	Non-randomised controlled trial	Clinical	38	Replace main meal with Glucerna SR (Glucerna® SR, Abbott Nutrition, Zwolle, the Netherlands/Chicago, IL) low GI (19)	PMR Provide 206 calories per 230 ml, with 9 g protein (20% kcal), 6 g fat (33% kcal) from monounsaturated-rich sources, 25 g (47% kcal) low glycaemic carbohydrate blend Blend with low calorie frozen yoghurt into 250-270 kcal	/	12 weeks
Steven et al. [3]	UK	Longitudinal study	Clinical	30	VLCD liquid diet Optifast (Nestle Nutrition, Croydon, U.K.)	TDR 3 shakes per day + 240 g non starchy vegetables 43% carb; 34% protein; 19.5% fat total Cal intake 624-700 kcal/day	/	8 weeks VLCD + 24 weeks wight maintenance phase
Shantha et al. [4]	USA	Cohort Study	Clinical	72	Calorie-restricted diet using meal replacements	1000 kcal/d energy deficit Individualized	Behaviour modification plan Plan to increase exercise with aerobic and strength training	Individualized 3 months to 1.5 years
Astbury et al. [5]	UK	Randomized controlled trial	Clinical	138	TDR with four formula products daily (LCD) provided by Cambridge Weight Plan UK	TDR First 2 weeks, liquid MR. Week 3 onwards MR bars option (soups, shakes, and bars), 750 mL of skimmed milk, 2.25 L of water or other low or no energy drinks, and a fibre supplement Energy intake comprised 810 kcal/day (3389 kJ/day)	/	8 weeks LCD, gradual food reintroduction, Weekly behavioural support for 24 weeks which one MR is consumed per day at this phase.
Baker et al. [6]	Australia	Non-randomized case-control trial.	Clinical	37	VLCD Optifast (Nestle Nutrition, Croydon, U.K.)	TDR 3 sachets Optifast (Nestle Nutrition) daily combined with serving of vegetable once daily (800 kcal/d) Purchased MR at cost price	After week 12, 8-week transition phase to calorie restriction diet based on Australian Commonwealth Scientific and Industrial Research Organization Total Wellbeing diet (1350 kcal) for another additional 4 weeks	12 weeks VLCD + 8 weeks transition to calorie restriction diet + 4 weeks 1350 kcal diet
Bishay, R [7]	Australia	RCT Protocol	Clinical	Not reported	VLCD Optifast	TDR 5-months of complete VLCD (820 KCal/day,) using Optifast® Phase 1: 3-4 meal replacements per day (months 1-3); Phase 2: 2 meal replacements plus one	/	32 weeks

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
						self-prepared healthy meal (month 4); Phase 3: 1 meal replacement + 2 self-prepared healthy meals (month 5); Phase 4: maintenance diet (months 6-8).		
Bhatt et al. [8]	India	Clinical Audit	Clinical	12	Low Calorie Diet TDR meal replacement protein formula [Prototal Whey)	TDR 1000 kcal/day diet containing 378.5 kcal, 48 g whey protein, 41 g of carbohydrate, and 2.5 g of fat along with micronutrients. Three servings (Breakfast, Lunch, Bedtime) of 30 g formula with 150 ml of skimmed milk in addition to one regular meal and 2–3 small prespecified homemade snacks.	/	12 weeks
Berk et al. [9]	Netherlands	Randomized controlled trial	Clinical	64	PMR with Very low-calorie diet Diabetes-specific meal replacement (Glucerna SR, Abbott Nutrition BV)	PMR Replace breakfast and lunch, light dinner for a combined 750 kcal/day	/	8 weeks + 12 weeks LCD reintroduction (1300 kcal/day)
Shiau et al. [10]	Canada	Retrospective cohort study	Clinical	317	Full meal replacement starting at week 2 - OPTIFAST ®900	TDR 4 MR shakes per day for a total of 900 kcal per day High in proteins (90g/day) and moderate in carbohydrates (67 g/day)	First 6 months - weekly diet session, behavioural and therapy Next 6 months - optional monthly support session	BMI of 33 kg/m2 or higher commit to 12 weeks of full MRs, while BMI below 33 start with 6 weeks of full MRs and the option to increase to up to 12 weeks of full MRs. 5 week transition to maintenance diet.
Cinkajzlová et al. [11]	Czech Republic	Intervention study	Clinical	22	VLCD	2500 kJ per day		
Taheri et al. [12]	Qatar	Non-blinded, randomised controlled, parallel-group trial	Clinical	70	LCD from the Cambridge Weight Plan	800 kcal benchmark First 12 weeks, consume mainly meal replacement products, supplemented by low-fat milk Month 4 to month 6, partial meal replacement plan and will be introduced to normal solid foods providing daily energy-based on body weight. Gradual introduction to three meal per day eating pattern.	Individual dietetic and activity appointments. Unsupervised physical activity of at least 150 min per week.	PHASE 1: 12 weeks LED + physical activity; PHASE 2: 12 weeks partial LED + physical activity; PHASE 3: 6 months own food, physical activity, and lifestyle change. PHASE 4: 12 months follow-up;
Harder et al. [13]	Denmark	Single arm study	Clinical	11	VLCD TDR with Liquid formula (Nutriletts NutriPharma, Oslo, Norway)	TDR 850 kcal/day containing 97 g protein, 81 g carbohydrate, and 15 g fat.	/	8 weeks

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
						Divided into eight portions, each containing 107 kcal, to be spread over the day		
Friedman et al. [14]	USA	Proof-of-concept pilot study	Clinical	6	PMR VLCD (Nutrimed; Robard Corporation, Mount Laurel, NJ)	PMR 800 kcal/d with at least 75 g of protein and all essential vitamins and nutrients. Four Nutrimed supplements (two 15-g protein bars and two shakes/smoothies/soups, one every 2–3 hours), one lean meal (two servings of vegetables and one serving of protein)	/	12 weeks
Lean and Leslie [15]	UK	RCT protocol	Clinical	Total N=25	TDR Low energy liquid formula diet (Counterweight Pro 800)	TDR Initial Total Diet Replacement phase (0-12 weeks) A commercial micronutrient-replete 825-853kcal/d LELD is provided (Counterweight Pro 800) to replace normal foods.	Counterweight-Plus' weight management programme Structured food reintroduction (12-20 weeks). -Replacing TDR with meals which contain 30% of energy from fat.	20 weeks with initial 12 weeks TDR
Wong et al. [16]	China	randomized, non-blinded, single center trial	Clinical	Total N=37	LED	PMR Replace at least one meal with less than 300 kcal	/	24 weeks
Leader et al. [17]	Australia	RCT	Clinical	36	PMR with Optifast VR	PMR Patients were randomized to receive 1 or 2 PMR/day	/	12 months
Overl et al. [18]	China	Conference paper RCT	NA	Total N=10	MR shakes	PMR Three meal replacement shakes (600 kcal/day) for two 24-hour periods/week.	/	12 weeks
Gulsin et al. [19]	UK	Single-center, prospective, randomized, open-label, blinded end point trial with a nested case-control study	Clinical	24	Low energy MRP from Cambridge Weight Plan	TDR~810 kcal/day (30% protein, 50% carbohydrate, and 20% fat) (Cambridge Weight Plan).	/	12 weeks
Farrer and Golley [20]	Australia	Non-randomized intervention	Clinical	19	Optifast VLCD programme	Three phases of 4 weeks each: Intensive (3 Optifast VLCD per day, <3360 KJ/day), Transition (2 Optifast VLCD per day, ~5040 KJ/day) and Maintenance (1 Optifast VLCD per day, ~5040 KJ/day) By 12 weeks, full normal meals were resumed	Traditional diabetes and weight management education	12 weeks

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
						according to meal plan to meet energy deficit requirements of 50% total energy .		
Sumithran and Proietto [21]	Australia	Case study	Clinical	1	TDR Optifast VLCD	TDR 5 months VLCD 3 times a day (1908 kJ) Transition phase 7 months: two VLCD meals per day and one low fat meal per day	Daily exercise program Weight control clinic	12 months
Roll et al. [22]	UK	Case study	Community	355	TDR with VLCD in the form of food packs (soups, shakes, textured meals and bars)	TDR 550 kcal daily 50 g protein, 50 g carbohydrate, mean 17 g fats, i.e., 36% energy from protein, 36% carbohydrate and 28% fat)	Commercial weight-management programme (LighterLife Total) Group support Cognitive behaviour therapy	12 weeks
Dhindsa et al. [23]	UK	Intervention	Clinical	44	TDR with VLCD Slimfast, liquid MR	TDR 3 Slimfast MR per day + One bowl of low-calorie vegetable soup, one bowl of vegetables or salad, two portions of fresh fruit and 300 ml of skimmed milk for drinks. 750 calories and 50 g of protein per day.	A follow-up phase (week 8 to week 52) in which a standard low-calorie weight-maintenance diet	i) 8 weeks of VLCD therapy (ii) A follow-up phase (week 8 to week 52) with a standard low-calorie weight-maintenance diet .
Khoo et al. [24]	Singapore	Randomized Trial	Clinical	19	PMR LCD liquid meal replacement (Kicstart, Pharmacy Health Solutions, Sydney, Australia)	PMR providing Maximum 450 kcal ,0.8 g/kg ideal body weight of protein and one other small meal, for a total of ~900 kcal/day for 8 weeks.	Switch to or continue on high protein diet for the remaining 44 weeks	8 weeks LCD/52 weeks
Moriconi et al. [25]	Italy	Retrospective study	Clinical	15	Very-low-calorie ketogenic diet (VLCKD) with MR from Therascience, New Penta SRL or Pronokal Group	First phase (45 days) TEI was < 800 kcal with 4/5 MR per day. Second phase (45 days), one and subsequently two replacement meals were replaced with conventional food. Carbohydrate intake drastically restricted at first two phases.	Subsequent phases caloric intake gradually increases, and full carb reintroduction is carried out until 6 months	Phase1 - 45 days Phase 2 - 45 days Phase 3 - until 12 months
Tang and Lin [26]	China	RCT	Clinical	50	PMR Fasting-mimicking diet (FMD) MR (Maide Technology Co., Ltd., Wuhan, China)	PMR Consumed FMD meal replacement from Monday to Friday in the second week of a month and ate normally for the rest of the month. The energy provision on the first day and the second to fifth days was 1196 and 805 Kcal, respectively (formula for patients weighing 75 kg).	/	MR for first 3 months and normal diet last months
Michelle et al. [27]	Ireland	Case study	Clinical	1	TDR with low-energy liquid diet, with 2.2 L of semi-skimmed milk	TDR 1012 kcal per day for 8 weeks divided in seven equal portions per day. (75 g of protein, 36 g of fat and 113 g carbohydrate)	/	8 weeks LELD + 16 weeks of phased reintroduction of normal diet

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
Nori Janosz et al. [28]	USA	Retrospective chart review	Clinical	33	Low Calorie Diet using partial meal replacements or complete meal replacement MR comprises of shakes, bars or prepared entrees.	PMR 1000-1200 kcal/day 47% carbohydrate, 34% protein, 18% fat	Behavioural treatment plan	At least 4 weeks
Storck et al. [29]	Germany	Prospective, interventional study	Clinical	36	TDR with balanced formula low calorie diet (OPTIFAST® II Short program, Nestlé Health Science, Germany)	Complete meal replacement with 5 sachets per day of 800 kcal for 6 weeks Contains an average of 96 g carbohydrates, 6.5 carbohydrate units (1.0–1.5 carbohydrate units per sachet), 70 g proteins, 15 g fat, and the recommended daily amounts of vitamins and minerals. 4 week refeeding phase where regular food was reintroduced. Last 5 weeks, energy intake will be gradually increased to between 1200 and 1500 kcal.	Standardized weight-loss program (OPTIFAST® II Short program, Nestlé Health Science, Germany) Weekly visit for exercise training. Diet counselling	12 weeks
Schwasinger-Schmidt et al. [30]	USA	Retrospective analysis	Community	44	TDR LCD in form of shakes, soups, cereal, and entrees	TDR Consume at least five meal replacements (shakes, soups, or cereal) along with two vitamin and mineral tablets per day. A minimum of 800 kilocalories per day	Weekly behavioural education classes	12 weeks
Steven and Taylor [31]	UK	Intervention study	Clinical	30	TDR VLCD liquid MR (Optifast)	TDR Replaced all meals with Optifast. 43% carbohydrate, 34% protein and 19.5% fat; vitamins, minerals and trace elements (624 kcal/day)	Discontinued all diabetic medications	8 weeks
Redmon et al. [32]	USA	RCT	Clinical	30	LCD MR (meal shakes or meal bars) from Slim Fast Foods Company	PMR Repetitive intermittent LCD weeks: LCD of 900–1,300 kcal per day (220 kcal/serving, four to six servings daily) for 7 consecutive days every 2 months On normal days, use one MR and one snack bar (120 kcal/snack bar) daily to replace one usual meal and snack to reach 500 to 1000 kcal per day reduction goal.	Combination therapy group Individual counselling by a registered dietitian Individualized diet that would promote a 500–1,000 kcal reduction in daily energy Individualized exercise prescription 10 mg sibutramine daily with the option to increase to 15 mg	12 months

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
							daily after 6 months if BMI remained >27 kg/m2	
Lips et al. [33]	Netherlands	Controlled nonrandomized observational trial	Clinical	12	TDR with Commercially available Prodimed (Prodimed Benelux BV, Val-kenswaard, The Netherlands)	TDR 4-5 sachets a day with 90 kcal each sachet, average 600 kcal/day 1 sachet: Approximately 18 g protein, approximately 2.5–5 g carbohydrates, 0.5–2 g fat	/	3 weeks
Elizabeth O Beale [34]	USA	RCT protocol	Clinical	15	TDR first 3 months PMR 3 -6 months HMR70 Plus products; HMR Boston, Massachusetts	Phase 1 consists of 3-months 1200 -1400 cal diet using full MR. Phase 2 consists of a 3-month transition to the same caloric intake using regular meals and 1 MR/day. Phase 3 consists of a 6-month weight loss maintenance period with 1 MR/day.	Usual care at Roybal Diabetes Management Clinic	12 months
Abi-Chahine et al. [35]	UK	Abstract for poster presentation for a person-centred intervention study	Community	23	TDR	12 weeks of Total diet replacement of 800kcal daily supplementation	Food reintroduction after 12 weeks Culturally sensitive diet and lifestyle support through 26 e-learning modules	24 weeks
Rafey et al. [36]	Ireland	Prospective observational cohort study	Clinical	20	Milk-based LELD	TDR Week 1 - 8: Semi skimmed milk in 7 portions per day. Approximately 1,200 kcal/day, or 130 g of carbohydrates and 40 g of fat intake per day. Week 9-16: gradual reintroduction of low calorie meals. Week 17-24: Stopped milk replacement and start fully isocaloric meal plan	/	24 weeks
Reynolds [37]	New Zealand	RCT protocol	Clinical	20	Cambridge Weight Plan products (VLED)	TDR Consumption of 3-4 meal replacements per day providing approx. 3600 kJ/day	Ongoing structured programme with monthly visits for long-term weight loss maintenance.	12 weeks
Scragg et al. [38]	UK	RCT protocol	Clinical	254	Low-energy low-carbohydrate diet	TDR 800-1000 kcal with a maximum of 40-60 g carbohydrate/day, compared to usual intake of 200-250 g	/	6 months
Tsompanaki et al. [39]	UK	RCT protocol	Community	28	TDR with LED	LED with package of soups, shakes, bars (4 per day providing ~850 kcal/day) for first 12 weeks	Stepped food reintroduction starting from 12th weeks and weight maintainence phase.	12 months
Shirmann [40]	UK	RCT protocol	Clinical	36	TDR with Low-calorie Diet Programme	Approximately 850 calories per day through four TDR products daily for 12 weeks Followed by a 6-week food reintroduction period and weight maintenance support for 8 months.	/	12 weeks

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
Hocking et al. [41]	UK	Single arm intervention trial	Clinical	155	TDR with LED Optifast; Nestlé Health Science	3 MRP per day (800 kcal per day). If BMI more than 40, 950 kcal per day.	Dieitian visits every 2 - 4 weeks.	13 week TDR 8 weeks structured food reintroduction 31 week supported weight maintainence
Ekberg [42]	Sweden	RCT Protocol	Not stated	286	Low Carb or low calorie diet	/	/	15 months
Otten [43]	Sweden	RCT Protocol	Clinical	106	TDR	TDR for 850 kcal/day.	Cognitive behavioural therapy program through face to face or ehealth application.	Total diet replacement for 3 months followed by weight maintenance for 21 months.
Anyiam et al. [44]	UK	RT	Clinical	18	TDR VLCD LighterLife® total meal replacement.	VLCD with less than 800 kilocalories per day		12 weeks
De Freitas et al. [45]	USA	Case study	Clinical	1	TDR VLCD with a formula liquid diet meal replacement	800 kcal/day Twelve weeks of VLCD were followed by 4 weeks of low-calorie diet (incorporating 3 meal replacements and 1 meal with ad libitum non-starchy vegetables)		16 weeks
Khoo et al. [46]	AUS	Retrospective cohort study	Clinical	51	PMR with LCD	Two meal replacement shakes plus a healthy meal.		3 months PMR + 21 months reduced calorie meal
Low Glycemic Index MR (n=6)								
Stenvers et al. [47]	Netherlands	Randomized, controlled, cross over trial	Clinical	29	Breakfast MR with liquid Glucerna GI=19	PMR Baseline breakfast intake mean 292 kcal	/	12 weeks
Foster et al. [48]	USA	Randomized controlled trial	Clinical	50	Pre-packaged, Portion Controlled Diet (Nutrisystem D, Fort Washington, PA, USA) (Three entrees and one snack) GI =35	PMR Women ~1250 and men 1550 kcal per day, respectively, with ~55% of total energy from the packaged foods and 45% from supplemental grocery items. The plans were structured to provide ~50–55% of energy from carbohydrate, 20–25% from fat and 20–25% from protein.	/	6 Months
Boonyavarakul et al. [49]	Thailand	Randomized controlled trial	Clinical	60	ONCE-PRO Replace one meal per day low-GI 27.99	PMR provides 30% of total daily energy requirement Protein:Fat:Carb - 20:30:50 To achieve 25–30 kcal/kg/day based on their ideal BW and physical activity	/	12 weeks
Di et al. [50]	China	randomized, open label,	Clinical	47	PMR Multi-nutrient powdered supplements,	PMR	All participants received diabetic health education	12 weeks

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
		intervention al study			which were provided by the LEHEL Company, Guangzhou, China. Low GI of 33 with high fibre	Consumes 75 g of the low glycemic index multi-nutrient supplement (provides 346 kcal energy) in place of breakfast	organized by nutritionists every 2 weeks	
Eliana and Agung Pranoto [51]	Indonesia	Randomized, controlled, crossover, open-labelled study	Clinical	30	TDR Carbohydrate mix-fortified liquid meal replacement nutrition (LMRN) GI = 32	TDR 4,008 kcal with a composition of 519.9 g carbohydrates, 156.74 g protein, 144.78 g fat, and 45.02 g fibre.	/	4 days x 2 (crossover) Washout 1 week
Santen et al. [52]	USA	Intervention Pilot study	Clinical	11	TDR with Nutrisystem®D® Meal Replacements, Nutrisystem Inc.	1450 to 1550 calories per day for men and 1200 to 1250 calories per day for women.	Telcare with glucometer, weighing scale and cloud data assessment. Education sessions.	Six months
Diabetes Specific Formulas (n=20)								
Belcaro et al. [53]	Italy	Single blinded RCT	Clinical	24	Partial MR with Glucaffect™ (Reliv Inc., Chesterfield, MO, USA)	PMR Substitute up to two meals a day for 6 days a week (8am to 6 am). Dinner following regular choices. 48 g powder per day	Personal Exercise Program with 60 minutes each day	8 weeks
Fonda et al. [54]	USA	Prospective, 3-way, cross-over design	Clinical	18	Glucerna Weight Loss Shake, Slim-Fast Shake, and Ensure with Fiber Shake	Subjects consumed the meal replacement beverages after an overnight fast, in random sequence on different weeks, 1 week apart (Figure 1), without taking their morning oral medications.	/	1 week
Garvey et al. [55]	UK	Multi-center, single arm, unblinded study	Clinical	147	/	PMR Two meal replacement shakes and snack bars daily	Diet and lifestyle counselling	12 weeks + 12 weeks sustainability
Sun et al. [56]	China	Unblinded, randomized, controlled clinical trial	Clinical	100	Breakfast replacement with Low glycemic diabetes-specific nutritional MR, Glucerna® SR.	PMR Replace breakfast, providing 200kcal, with 25 g carbohydrate, 10g protein, 7g fat, 3g dietary fibre.	Weekly sessions on: Diet consultation Review of blood glucose measurements	24 weeks
Peng et al. [57]	China	RCT	Clinical	62	PMR breakfast with Glucerna SR (Abbot Nutrition)	PMR Replacing breakfast providing 220.5 kcal, 29.1 g of carbohydrate, 11.0g of protein and 8.0 g fat.	Lifestyle education Prescribed an individualized meal plan to ensure total daily caloric intake of 25-30 115 kcal/kg ideal body weight (IBW)/day	4 weeks

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
Chee et al. [58]	Malaysia	RCT	Clinical	115	PMR Diabetes-specific MR (Glucerna SR, Abbott Nutrition, USA)	PMR Structured low-calorie meal plan - 1200 or 1500 kcal/day Normal foods + one or two diabetes-specific formula servings	ten group receives physical activity at least 150 min/week Education using tDNA toolkit: Flipchart on healthy eating, 14-day meal plans, information on PA Subgroup receives motivational interviewing or conventional interviewing	6 + 6 months fup
Patel [59]	India	RCT Protocol	Clinical	100	PMR Prohance D Vanilla Flavour (Nutraveutical Product)	Prohance D Vanilla Flavour (Nutraveutical Product): once a day	/	12 weeks
Hwu [60]	Taiwan	RCT procotol	Clinical	30	PMR Glucerna SR	Glucerna SR to replace one meal (breakfast) and one pre-sleep snack for 24 weeks.	Diet plan with 500 ~ 800 kcal/day less than their estimated daily maintenance energy requirement	24 weeks
Bao [61]	China	Single-center, Randomized, Open-label, Parallel Group Study Protocol	Clinical	66	PMR Breakfast with Glucerna SR	To replace breakfast	/	4 weeks
Lansink et al. [62]	Netherlands	Randomized, controlled, double-blind, parallel-group study	Clinical	22	PMR with Diabetes-specific formula - Diasip® (Nutricia N.V., Zoetermeer, The Netherlands)	Consumed two 200 mL portions (200 kcal per portion) per day of either of the products for 4 weeks, one as a replacement for breakfast and one as an in-between snack in the afternoon or evening. MR 1kcal/ml (47 En% carbohydrates, 19 En% protein, 34 En% fat (20 En% monounsaturated fatty acids) and 2 g fibers/100 mL)	/	4 weeks
Mottalib et al. [63]	USA	A prospective, randomized, three-arm study	Clinical	72	PMR Diabetes specific nutrition formula (DSNF)	Group B and C - hypocaloric dietary plan (1500 kcal/day for women, 1800 kcal/day for men) that included use of a commercially available diabetes specific nutrition formula (DSNF) 1–3 times per day within their caloric limit. DSNF had 220 kcal/serving and contained 32.7% calories from fat, 40% calories from carbohydrate, and 27.3% calories from protein.	/	16 weeks
Otto et al. [64]	Canada	Retrospective cohort study	Clinical	47	Liquid MR Glucerna	2 cans of Glucernaä per day (each can provide 230 kcal, 30 g carbohydrate, 11 g protein, 8 g fat) as part of a 1200 to 1400 calorie diet.	/	At least 3 months
Yip et al. [65]	USA	RCT	Clinical	41	PMR Liquid MR preparation containing	MR1 (Slim-Fast Foods, New York, NY) contained 11 g of lactose, 13 g of fructose, 8.5 g of sucrose, and 14	/	12 weeks

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
					lactose, fructose, and sucrose (Slim-Fast; MR1) Liquid MR in which sucrose and fructose were replaced by nonsugar-containing glucose oligosaccharides (sugar-free Slim-Fast; MR2)	g of protein. MR2 was identical to MR1, but fructose and sucrose were replaces with equivalent levels of maltodextrins. (250 kcal each) Replaced their three meals with MRs for the first 5 days. Replaced two meals for remainder of the study		
Mottalib et al. [66]	USA	Cross-over, three-way and open-label clinical study	Clinical	22	Three type of meal replacement served on each visit on breakfast: Glucerna (Abbott Nutrition Inc., Columbus, OH, USA) Ultra Glucose Control (Metagenics Inc., Aliso Viejo, CA, USA) OM (Quaker Oats Co., Chicago, IL, USA)	200kcal/meal	/	Three visits with crossover of different MR
Cheskin et al. [67]	USA	Controlled clinical trial	Community	54	PMR Medifast Plus for Diabetics (Medifast, Inc, Owings Mills, MD) meal replacements (portion-controlled diet [PCD])	25% of energy calorie deficit at weight-loss-phase diet, and a 10% calorie deficit at weight-maintenance-phase diet. PCD group received approximately 50% to 60% of their prescribed calories from meal replacements Diets of similar macronutrient composition: 45% to 50% carbohydrate, 25% to 30% fat, and 15% to 25% protein	After an initial 34-week weight loss period, PCD participants were rerandomized for their 52-week maintenance phase to either 26 weeks of PCD followed by 26 weeks of Standard Diet (PCD1) or vice versa (PCD2).	34-week weight loss period and 52-week maintenance phase (86 weeks)
Mustad et al. [68]	USA	randomized, open-label, three-group parallel study design	Clinical	49	PMR with Diabetes Specific Nutritional Shakes - Glucerna Hunger Smart (Abbott Nutrition, Columbus, Ohio).	One meal supplies 180 kcal. DSNS breakfast and afternoon snack (Bkfst/AS) (n=24) DSNS breakfast and bedtime snack (Bkfst/PBS) (n=25) Self-selected diets for 7 days, then MR for 7 days.	/	7 SSD+7 days MR
Lew et al. [69]	Malaysia	RCT Protocol	Clinical	78	PMR with Diabetes specific meal replacement - Metabolic Sauver, Powerlife (M) Sdn Bhd,, Kuala Lumpur, Malaysia.	Comsume PMR for 5 days a week replacing 1 meal per day, providing 327 kcal per comsumption.	Dietary Consultation	12 weeks intervention + 12 weeks follow up

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
Wichansawakun [70]	Thailand	RCT Protocol	Not stated	76	PMR with Diabetes specific meal replacement	Replace 1 meal per day based on weight based calculation at 25-30 kcal of energy per ideal body weight per day, and the ratio of carbohydrates to protein to fat is 45-50:20. :30-35 of total energy.		12 weeks
Dharmalingam et al. [71]	India	RCT	Clinical	71	PMR with DSNS (Prohance-D® Vanilla flavored powder) Sun Pharmaceutical Industries Limited, Mumbai, India	One serving of DSNS used as breakfast/evening snack replacement, providing 16.8% of the recommended daily allowance (RDA) of protein, 454kcal energy.	Oviva Diabetes Remission Insulin (ODR-I) programme: - expert dietitian coaching - Oviva app (with a 12-month weight prediction chart) - Capilar Blood Glucose meters (for enhanced safety in view of concerns re hypo- and hyper-glycaemia) - BodyTrace weight scales.	12 weeks
Zagury et al. [72]	Brazil	Randomized control crossover trial	Clinical	34	Glycemia targeted specialized supplement PMR Nutren Control® , Nestle.	Replaced breakfast to provide 208 kcal	/	7 days
Protein Rich MR (n=13)								
Keogh and Clifton [73]	Australia	Randomized controlled trial	Community	60	Protein-rich MR Probiotec Formula WL (Probiotec Limited, Laverton North, VIC, Australia 3026)	2 MR (880kJ each) and low-fat evening meal per day first 12 weeks + at least 5 serves of fruit and vegetables/day (total approximately 5000 kJ) 1 MR for further 12 weeks	/	24 weeks
Navas-Carretero et al. [74]	Spain	Single group, sequential, longitudinal design	Clinical	17	4 weeks Structured meal replacements: Breakfast, morning snack and afternoon snack, were exchanged by specific products, with a moderately high protein content and low glycemic index (55) Enerzona© (Equipe Enervit)	40-30-30: proteins-carbohydrates-lipids. ~1800 kcal	/	4+4 weeks
Manjunath [75]	India	Randomized, Parallel Group, Multiple Arm Trial Protocol	Clinical	120	PMR Almased Soya protein powder with yogurt	During the first 6 months, Almased (Soya protein powder with yogurt, diluted with 250 ml of water) will be given as a meal replacement substituting one major meal/day; the dosage will be defined individually according to body weight. During the next 6 months, Almased (50 g/d) will be added to the diet before one meal.	/	6+6 months FUP

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
Kempf et al. [76]	Germany	Proof of principle study	Clinical	22	Protein Rich Meal Replacement (Alm-ased-Vitalkost; Almased-Wellness-GmbH, Bienenb€uttel,Germany)	First week, Breakfast, lunch and dinner replaced with Almased (50 g per meal = 150g per day = 2223 kJ) + 45 g oil (1717 kJ) + 750 ml vegetable juice (544 kJ), Total 4903 kJ per day. 2 - 4 week: Breakfast and dinner (1465 kJ) + regular lunch (2093 kJ) + 45g oil, total 4600 -5300 kJ 5 - 12 week, only dinner is replaced with 50g Almased.	/	12 weeks
Kempf et al. [77]	Germany	RCT	Clinical	Strict diet regime N=37 Moderate group N=43	PMR Almased®, Almased-Wellness-GmbH, Germany	Strict diet group replaced three meals in week 1, two meals in weeks 2-4 and one meal in weeks 5-12 with 1g PMR (Almased®) per kg normal body weight. Moderate group replaced two meals in weeks 1-4 and one meal in weeks 5-12.	/	12 weeks + 9 months follow up
Kempf et al. [78]	Germany	Conference paper RCT	Clinical	55	PMR with Protein-rich meal replacement	/	/	12 weeks
Martin et al. [79]	Germany	RCT	Clinical	stringent diet regime (n=40) moderate diet regime (n=37)	PMR (Almased-Vitalkost, Almased Wellness GmbH, Bienenbüttel, Germany)	Stringent Group: 1st week: Replaced 3 main meals by 50 g PRMR = 1100 kcal/day 2-4th week: 2 meals were replaced, and a protein-rich lunch was allowed 5-12th week: only dinner was replaced.	Moderate Group: Replaced breakfast and dinner for 5 weeks and then only dinner during the next 7 weeks.	12 weeks
Li et al. [80]	USA	RCT	Clinical	46	PMR with Soy protein MR (Slim Fast Food Company, Inc. West Palm Beach, FL 33401, USA)	Replace 3 meals per day for first 5 days of the study. Replace 2 meals for three additional months. After three months, replace one to two meals per day with MR.	/	12 months
Kempf et al. [81]	Germany	Single-blind, active comparator, intervention study	Clinical	102	PMR (Almased-Vitalkost, Almased Wellness GmbH, Bienenbüttel, Germany)	1st week: Replaced 3 main meals by 50 g PRMR = 1100 kcal/day 2-4th week: 2 meals were replaced, and a low carb protein-rich lunch was allowed 5-12th week: only dinner was replaced.	Weekly care calls (planned duration 20 min) from trained diabetes coaches. Received a weighing scale, and a step counter; the TeLiPro group additionally received a blood glucose meter.	12 weeks 26 week and 56 week follow up without intervention
Shirai et al. [82]	Japan	Randomized Trial	Clinical	119	PMR with Protein Sparing Formula Diet (Microdiet, Sunny Health Co. Ltd)	One pack of MR in the morning providing 240 kcal/meal 2 conventional Japanese meal in noon and evening	/	24 weeks

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
						Protein:fat:carbohydrate ratio was 18:30:52		
Durrer et al. [83]	Canada	RCT Protocol	Clinical	100	Commercial diet plan (Ideal Protein) with pre-packaged foods used for two meals and one snack each day, with the third meal being prepared from a select group of lower-fat protein sources (e.g., meat, eggs) and low-carbohydrate vegetables.	The macronutrient composition of the meal plan equates to < 50 g of carbohydrates, ~ 35-45 g of fat, and ~ 110-120 g of protein for a total of approximately 850–1100 kcal per day.	/	12 weeks
Kerstin et al. [84]	Germany	RCT	Clinical	M: moderate diet group 146 S: stringent diet group 139	PMR Formula diet (Almased-Vitalkost; Almased-Wellness-GmbH, Bienenbüttel, Germany)	Contained 30.6 g carbohydrates and 1507 kJ (360 kcal) energy per 100 g powder. Week 1: Both intervention groups replaced breakfast, lunch, and dinner with 1 g Almased/kg normal body weight per meal and consumed 45 g of oil rich in omega-3-fatty acids (1665 kJ; 398 kcal) and 750 mL vegetable juice. Weeks 2–4: the participants replaced breakfast and dinner with the formula diet and ate a low-carbohydrate lunch. Week 5-12: Only dinner was replaced by formula diet, continues low carb diet. All of the participants were asked to continue replacing one meal per day during the follow-up period until the final visit at the 52-weeks follow-up	The only difference between both intervention groups was that the M-group should only replace two meals per day during the first week	12 weeks of intervention, and 52 weeks of follow-up
Papakonstantinou et al. [85]	Greece	Randomized, crossover Protocol	Clinical	17	PMR Optifast by Novartis Hellas, S.A.C.I., Metamorfossi, Greece	Replaced breakfast and lunch and made up 26% of their energy intake.	/	/
Low Fat MR (n=1)								
Barbosa-Yañez et al. [86]	Germany	randomized, parallel group, intervention study	Clinical	43	Low Fat Diet TDR Flavoured meal replacement powder (MODIFAST®(OTC Siebenhandl GmbH)) Ulm,Germany))	TDR 1000–1200 kcal/day, and less than 30% of the total energy intake (E%) is fat 200 g of raw or steamed vegetables	/	3 weeks of intensive low fat diet, 49 weeks of eucaloric diet under DGE guidelines
MR + Lifestyle Intervention Programme (n=11)								
Delahanty et al. [87]	USA	Randomized, assessor-blinded,	Clinical	69	PMR (shakes, bars, and pre-packaged entrees)	Use of meal replacements was recommended (but not supplied by the study) for 1–2 meals per day starting in week 3 based on the Look AHEAD	LI delivered by registered dietitian with 37 session identical contents in in-person	12 months

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
		practice-based clinical trial				protocol. Meal replacement use was not formally tracked.	and telephone arm. Content was a curated hybrid of key publicly available English and Spanish DPP and Look AHEAD session materials minimally modified for delivery in groups of 4–12 participants with decreasing intensity over 2 years. MNT participants were referred to a dietitian at their health center or preferred location and were counselled regarding MNT's proven effectiveness for weight loss and improved diabetes control. The number of MNT visits was determined after the initial visit by the dietitian and the participant as per usual care	
Wycherley et al. [88]	Australia	Randomized clinical trial	Community	37	PMR Liquid MR (KicStartä, Pharmacy Health Solutions, New SouthWales, Australia)	High-protein, energy-restricted diet (5500 kJ/day) Two meal replacements added to 200 ml of skim milk (47% of total energy as protein, 41% as carbohydrate and 12% as fat) and one self-prepared high-protein meal.	A group of only diet. Another group of Diet + exercise Walking/jogging exercise programme comprising four to five exercise sessions per week	12 weeks
McDiarmid et al. [89]	UK	RCT	Clinical	79	LED TDR Optifast 820	8 weeks of Optifast 820 kcal/3430 kJ formula diet, followed by 4 weeks of food reintroduction.	Both groups were asked to complete 56 Optifast 820 kcal/3430 kJ days during their active weight loss phase with an equivalent energy deficit. Then the participants will be separated into two groups with CLED following a portion-controlled Mediterranean diet 7 days per week while ILED follows a MR diet for 1-2 days and portion-controlled Mediterranean diet for 5-6 days a week.	12 months
Reynolds et al. [90]	USA	RCT	Clinical	21	PMR Prepackaged entrees and low calorie shakes (Health Management Resources, Boston, MA)	Replace two meals with at least 1500 kcal per day	Placebo or RSG 4mg/day Lifestyle programme with weekly behavioural education	6 months

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
							classes for 6 weeks then bi-weekly classes for remainder of the study.	
Hamdy and Carver [91]	USA	Intervention study	Clinical	85	Nutritionally complete MR to replace breakfast and lunch - BOOST Glucose Control (Nestlé HealthCare Nutrition, Inc., Minneapolis, MN).	Each participant received a meal plan with a 500-calorie reduction rounded to the nearest 1200-, 1500-, or 1800-calorie level. Meal plans were developed according to the Joslin Nutrition Guidelines for obese diabetic patients to provide approximately 40% of daily caloric intake from carbohydrate, with a total daily intake of no less than 130 g/d, 30% from protein (to minimize lean-mass loss during weight reduction), and the remaining 30% from fat.	Weekly cognitive behavioural support Weekly group education Intensive and interactive diabetes medication adjustment Individualized exercise plan	12 weeks
Pi-Sunyer et al. [92]	USA	RCT	16 Clinical Centres	2496 (97.1%) ILI 2,463 (95.7%) DSE	Liquid Meal Replacement and Meal bars 4 Meal replacements to choose from (FOC): Slim Fast (Slim Fast Foods), Glucerna (Ross Laboratories), OPTIFAST (Novartis Nutrition) and HMR (HMR, Inc.).	First 3 weeks: Self-selected diet which energy goal for persons < 114 kg is 1200−1500 kcal/d and is 1500−1800 kcal/d for individuals ≥ 114 kg. First 6 months: Replace two meals and one snack a day with liquid shakes and meal bars. (1200−1500 kcal/d) Months 7 onwards to year 4: Replace one meal and one snack per day Calorie targets personalized based on participants weight loss goals	1 hour diabetes education class on first visit + Three group educational/social support sessions each year for 4 years **Lifestyle intervention:** **Diet modification:** First two weeks self-selected food with calorie goal of 1200–1500 kcal/day for < 250 pounds, or 1500–1800kcal/day > 250 pounds. At session three: Structured dietary program of 2 MR+1 portion-controlled snack+1 self-selected meal At week 20: 1 MR per day and 2 self-selected food Year 2-4: 1 MR per day **Physical activity:** Unsupervised exercise with 175 minutes of moderate intensity PA per week at end of first 6 months. (5 days per week) **Behavioural techniques:** Participants who fail to lose at least 1% of body weight	Intensive intervention for first 4 years, with an average of 10.25 years follow up.

Author/Year	Country	Trial Type	Setting	Meal Replacement Arm (n)	Meal Replacement Type	Dosage/Calorie	Combination	Length of intervention/follow up
							per month during the first 6 months will be given special assistance by lifestyle counsellor and provided Orlistat on those who are medically appropriate.	
Lean et al. [93]	UK	RCT	Clinical	149	Total diet replacement using LED (Counterweight-Plus MR)	TDR phase using a low energy formula diet. (825–853 kcal/day)	Counterweight-Plus weight management programme	Total diet replacement of 3 - 5 months with stepped food reintroduction of 2-8 weeks and long-term weight maintenance program until month 12
Sattar et al. [94]	UK	RCT	Clinical	25	TDR with Low energy liquid formula diet (Counterweight Pro 800)	Initial Total Diet Replacement phase (3-5 months) A commercial micronutrient-replete 825-853kcal/d LELD is provided (Counterweight Pro 800) to replace normal foods.	Counterweight-Plus' weight management programme Structured food reintroduction (6-8 weeks).	3 months minimum
Marples et al. [95]	UK	Intervention study/service evaluation	Clinical	37	Phased LED TDR and PMR with Counterweight TDR products	TDR phase: 825–853 kcal/day Food reintroduction phase: Gradual reduction in the formula product and the incorporation of nutritionally dense and energy-restricted meals (360–400 calories per meal). Weight Loss Maintenance phase	Behhaviour change techniques	TDR phase: 12 weeks Food reintroduction phase: 9 weeks Weight Loss Maintenance phase: 31 weeks
Dasgupta et al. [96]	UK and Canada	RCT protocol	Clinical	50	Phased TDR and PMR with Optifast products (Nestlé)	First 2 weeks: Optifast products (Nestlé), totalling 800–900 kcal/day (30% protein, 50% carbohydrate and 20% fat). Week 3-12: PMR with 800–900 kcal daily on non-exercise days and an additional 150–200 kcal from meal replacement products on exercise days. Week 12-24: Maintainence phase, individualized meal plan	Exercise training	24 weeks : 12 weeks MR and 12 week maintainence

Supplementary Table 6 Outcome of MR on HbA1c, Glucose, Weight, Other Health Status and Adverse Effects

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
Low Calorie/Energy MR (n=37)							
Rothberg et al. [1]	2014	HbA1c reduced 0.9% at established T2DM patients (++)	/	Decreased BMI by 5kg/m2 (+)	/	/	Not reported
Tatti et al. [2]	2010	Greater reduction in HbA1c after 3 months treatment compared to group without meal replacement (8 ± 1.65 to 6.7 ± 0.88) (p<0.0001) (++)	Reduction in blood glucose level (+)	Significant reduction in body weight compared to previous 3 months (88.7 ± 9.6 to 77.5 ±10) (p<0.0001) (++)	Significant reduction in TC, TG. Significant increment in HDL.	Significant reduction in bp (++)	Not reported
Steven et al. [3]	2016	Reduced significantly in responders and reduced in non-responders and remaining constant at 24 weeks. (++)	40% responded to VLCD and achieve FPG <7mmol/L for at least 6 months (++)	Reduced significantly (15kg) in both groups (++)	Improved lipid profile but not significant (+)	Plasma insulin levels reduced in both groups after the VLCD and remained stable throughout the weight maintenance phase (++)	Not reported
Shantha et al. [4]	2012	All achieved at least 0.5% hba1c reduction (+)	/	Significant mean weight loss (10.7 kg) (++)	/	/	Not reported
Astbury et al. [5]	2018	Reduced -8.5 ± 17.8 mmol/mol (p=0.9885) (+)	Reduced -1.7 ± 3.9 mmol/L but not significant (+)	Significantly reduced -10.7 kg (++)	No changes in lipid profile (=)	Significantly improved HOMA-IR (-1.1± 2.3)	69 (51%) participants in the TDR group. The most common adverse events where there was a greater incidence in the TDR group were constipation (1 in 7), fatigue (1 in 12), headache (1 in 17), and dizziness (1 in 22).
Baker et al. [6]	2011	/	/	−8.5 ± 1.3 kg significant reduction (++) −3.0 ± 0.5 BMI significant reduction (++)	/	Fasting plasma insulin concentrations were decreased at week 2 compared with baseline in both diabetic and control (both P< .001) and remained significantly lower than baseline values in the diabetic group at all time points to week24 inclusive (all P < .01)	Not reported
Bhatt et al. [8]	2017	All participants (n = 12) had a significant fall in their HbA1c (median HbA1c dropped from 9% to 6.2%) (++)	Significant reduction in FBG in both responders and non-responders. (++)	Significant reduction in weight and BMI for both Responders: 83 - 76.5 Non-R: 84.5 - 78.5 (++)	Improved TG in responders significantly. Others no changes (=)	/	Not reported
Berk et al. [9]	2016	7.8% - 7.2% (p<0.001) (++)	8.8 - 7.2 (p<0.001) (++)	Weight: 106.7 ± 19.5 - 96.3 ± 17.7 (p<0.001) Bmi:	Total CHO: 4.5 - 4.3 (p=0.003) HDL: 1.1 - 1.2 (P=0.003) LDL: 2.5-2.5 (p=0.035) TG: 1.9-1.5 (p<0.001)	Plasma sLR11 levels were significantly reduced in overweight and obese individuals (p<0.001) Positively associated with	Not reported

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
				37.2±5.3 - 33.6±5.0 (p<0.001) (++)	Non-HDL Cho: 3.3 -3.0 (p<0.001) (++)	changes in non-HDl cho and HbA1c	
Shiau et al. [10]	2017	7.5% - 6.7% (p<0.0001) (++)	/	16.7% weight loss (p<0.0001) (++)	/	/	Not reported
Cinkajzlová et al. [11]	2017	/	VLCD reduced FPG -2.05 mmol/l (Sig vs Obesity vs Control vs pre) (++)	VLCD reduced BMI 50.0 - 46.9 (Sig vs Control vs pre) (++)	Improved CHO, TG, HDL, LDL (Sig vs Control vs pre) (++)	/	Not reported
Taheri et al. [12]	2019	The reduction in mean HbA1c between baseline and 12 months was greater in the intervention group (-0.89) than in the control group (-0.35) (adjusted difference −0·62 [95% CI −0·92 to −0·33], p=0·020) (++)	/	Mean bodyweight of participants in the intervention group reduced by 11·98 kg (95% CI 9·72 to 14·23) compared with 3·98 kg (2·78 to 5·18) in the control group (adjusted mean difference −6·08 kg [95% CI −8·37 to −3·79], p<0·0001) (++)	Mean TC and mean LDL increased at 12 months in the intervention group. (-) Mean HDL and TG improved at 12 months but not significant. (+)	Diabetes remission occurred in 61% of participants in the intervention group compared with 12% of those in the control group (odds ratio [OR] 12·03 [95% CI 5·17 to 28·03], p<0·0001). (++) Intervention group have improved quality of life.	Compared with the control group, more participants in the intervention group reported dizziness, constipation and other gastrointestinal symptoms, hair loss, and fatigue
Harder et al. [13]	2003	Reduced significantly (-1.0%) (p=0.006) (++)	Reduced significantly from 8.1 ± 0.7 to 6.4 ± 0.4 (p=0.05) (++)	Reduced significantly from 100.6 ± 4.7 kg to 89.3 ± 4.3 kg (p<0.001) (++) Mean weight loss was 10.9 kg, ~11% of initial body weight	TC fell by 20% (P<0.001), LDL by 17% (P<0.05), and TG by 39% (P<0.05). (++)	/	Not reported
Friedman et al. [14]	2013	Reduced from 7.2 to 6.4 (++)	Significant improvement in FBG (166 vs 131 mg/dl, P<0.05) (++)	Significant reduction in weight (118.5 vs 104.3 kg, p<0.05). (++) BMI reduced from 38.6 to 34.0 (p<0.05) (++)	/	A statistically significant approximately 12% reduction in serum creatinine, cystatin C and eGFR. A 36% reduction in albuminuria	The only adverse effects noted were transient elevations in BUN and serum creatinine early in the diet that resolved after reducing the doses of antihypertensive medications.
Lean and Leslie [15]	2017	A greater mean HbA1c reduction of 0.53% (+/- 0.81%, P = 0.013) was achieved in MR (++)	/	Mean weight loss was 1.81 kg (+/-2.85 kg) and 1.89 kg (+/- 2.37 kg) at 12 and 24 weeks respectively in MR (P = 0.015) (++)	/	/	Not reported
Leader et al. [17]	2012	At 3 months, both groups had a significant reduction HbA1c compared with baseline. (++) Group with 2 PMR has better reduction in HbA1c	/	At 3 months, both groups had a significant reduction in weight compared with baseline. (++) Patients on 2 PMR/day lost almost 4 kg compared with only 0.5 kg in the 1 PMR/day group.	/	/	Not reported

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
Overl et al. [18]	2017	HbA1c is reduced significantly in the MR cohort (p<0.1) (++)	/	Weight is reduced significantly in the MR cohort (p<0.1) (++)	/	/	Not reported
Gulsin et al. [19]	2020	Median HbA1c decreased by 0.75% (7.5 mmol/mol), with 20 (83%) participants achieving T2D remission. (++)	/	Reduction of 13.6 kg (++)	/	Improved blood pressure, LV mass/volume, and aortic stiffness.	Not reported
Farrer and Golley [20]	2013	A significant change in HbA1c over 12 weeks was observed for the treatment group with an overall change of -1.48%. (++)	/	The 6.6 kg average weight loss in the treatment group was significantly greater (P=0.004). (++) The change in BMI was also significantly greater in the treatment group. (++)	No significant changes in cholesterol (=)	/	Not reported
Sumithran and Proietto [21]	2008	Reduced from 12.2 to 4.7 % on 12th month (++)	FBG reduced from 12.5 to 4.5 at month 12 (++)	Lost 43% of initial weight and was down to 96.5 kg (BMI, 26.7 kg/m2) (++)	/	/	Not reported
Roll et al. [22]	2013	/	/	Significant weight reduction at week 12 (115.0±24.4 kg vs. 96.7±21.4 kg,P<0.0001). (++)	/	/	Not reported
Dhindsa et al. [23]	2003	Short term: Favourable reduction of Fructosamine (386 ± 73–346 ± 49 µM) (equates to an HbA1c reduction of approximately 1%). Long term: Mean fructosamine: 371 ± 41 µM (++)	/	Short term: The average weight loss was 12 kg, and mean BMI had fallen from 40 to 36 kg /m². Long term: Average body weight and BMI after 1 year were 109.5 kg and 37 kg/m2 (++)	Short term: Improvements in serum lipids (e.g. 1.0 mmol/ l reduction in total cholesterol) (++)	Reduction in BP (average reduction 10/6 mmHg)	Not reported
Khoo et al. [24]	2011	/	Plasma glucose and LDL decreased significantly in both groups. LCD (7.42 ± 0.59 to 6.54 ± 0.46 mmol/L) (Significant difference from baseline) (++)	Mean weight loss greater in LCD group (~10%) (112.7 to 103.2 kg, p < 0.05) than in the High Protein diet group (~5%). (++) At 52 weeks, weight loss was maintained in both groups.	Significant reduction in LDL	Quantitative Insulin Sensitivity check, SHBG, IIEF-5, SDI, IPSS scores and endothelial function improved significantly in both diet. Erectile function, sexual desire, and urinary symptoms improved by a similar degree with both diets.	Not reported
Moriconi et al. [25]	2021	At T1, HbA1c was decreased by 0.69 ± 0.65% in the VLCKD group. At T2 the change in HbA1c	/	In the VLCKD group, a significant weight-loss was observed at 3 (8.5% from baseline, p = 0.000)	Total cholesterol decreased in the VLCKD group at all timepoints (++).	Systolic blood pressure was significantly decreased at T1 and T2 in VLCKD group.	Not reported

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
		from baseline was 0.61 ± 0.54% in the VLCKD group. (++)		and 12 months (11.5% from baseline, p = 0.000)(++)			
Tang and Lin [26]	2020	Hba1C reduced from 7.83 to 6.47 % (p<0.001) (++)	FPG reduced from 7.56 to 5.25 mmol/L (p<0.001) (++)	BMI reduced from 30.15 to 25.04 (p<0.001) (++)	Improved TC, TG, HDL-C and LDL-C significantly (++).	/	Not reported
Michelle et al. [27]	2019	HbA1c normalised 6 months after intervention (+)	/	Weight reduction from 115.2 kg (BMI: 40.7 kg/m2) to 101.2 kg (BMI: 35.8 kg/m2) after 8 weeks and 94.6 kg (BMI: 33.4 kg/m2) after 24 weeks, a reduction of 20.6 kg (7.3 kg/m2) (++)	/	/	Not reported
Nori Janosz et al. [28]	2008	All cases had final HbA1C values < 6.0% (Achieving resolution of T2DM) (++)	No significant paired differences in fasting blood glucose in cases and controls (=)	The absolute and relative reduction in BMI was 7.6 ± 3.7 kg/m2 and 18.1 ± 8.2% in cases vs. 3.9 ± 3.7 kg/m2 and 8.5 ± 8.0% in controls, respectively, (p < 0.0001 for both comparisons) over a mean duration of 11.2 ± 4.9 and 14.9 ± 13.0 months for cases and controls (++)	/	/	Not reported
Storck et al. [29]	2021	Reduction of -0.5% (p<0.001) (++)	Reduction of -0.9 mmol/L (p=0.02) (++)	Weight -11.9kg from baseline (p<0.001) (++) BMI -4.1 (p<0.001) (++)	TG decreased significantly by 32% (p = 0.003) and TC by 46% (p = 0.003) (++)	WC -11cm (p<0.001) Surrogate markers of liver function, namely ALT, AST, and γ-GT, decreased significantly Insulin and HOMAIR improved, but not significant.	Five patients reported constipation.
Schwasinger-Schmidt et al. [30]	2020	1.03 ± 1.38 % reduction at week 12 but non-significant (+)	Reduction of -17.03 ± 78.27 mg/dL from baseline but not significant. (+)	11.28 ± 10.96 kg reduced from baseline level (p=0.0211) (++)	/	/	Not reported
Steven and Taylor [31]	2015	HbA1c reduced from 7.2 ± 0.2% to 6.1 ± 0.2% in the short-duration group (P<0.001) and from 8.6 ± 0.4% to 8.0 ± 0.5% in the long-duration group (P=0.276). (++)	FPG reduced from 9.6 ± 0.7 to 5.8 ± 0.2 mmol/l in the short-duration group (P<0.001) and from 13.4 ± 0.8 to 8.4 ± 1.1 mmol/l in the long-duration group (P<0.001). (++)	Weight loss in short duration is 99.0 kg to 84.5 kg while in long duration is 96.9 kg to 83.0 kg. (++)	Clinically significant improvements in lipid profile regardless of diabetes duration (++)	/	Not reported
Redmon et al. [32]	2003	HbA1c decreased 0.6 ± 0.3% in the combination	Reduction in glucose level (-12 ± 9 mg/dL) but not	At 1 year, weight loss in the combination therapy group was 7.3 ± 1.3 kg (P <	Reduction in fasting triglycerides, cholesterol	/	Dry mouth and constipation were reported by some subjects

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
		therapy group (P = 0.05) (++)	significant between group (++)	0.001) At 1 year, the mean weight loss of 7.3 kg in the combination therapy group resulted from a net weight loss of 7.7 kg during the 6 low-calorie diet weeks and a net weight gain of 0.4 kg during the six intervening periods Decreases in BMI, fat mass, and lean body mass significantly greater in combination therapy group than in standard therapy group. (++)	and LDL but not significant (+)		on initiation of combination therapy. Some subjects in the combination therapy group experienced mild hypoglycemia during low-calorie diet weeks.
Lips et al. [33]	2014	/	RYGB and VLCD induced a comparable decline in fasting and postprandial glucose levels. (++)	VLCD reduced weight in T2DM patients from 112kg to 105.3kg after 3 weeks (++)	/	Fasting insulin levels decreased only after VLCD. Homa-ir significantly decreased after VLCD, but not after RYGB (++)	Not reported
Abi-Chahine et al. [35]	2021	Mean HbA1c decreased by 14 mmol/mol at week 24 but was only available for 11 participants. (+)	/	Mean weight loss after TDR was 13.5 kg (range 5-29 kg) at week 24. (++)	/	Self-reported improvement in participants' quality of life	Not reported
Rafey et al. [36]	2022	HbA1c decreased from 60.0 ± 17.4 to 47.5 ± 15.5 mmol/mol (p < 0.001) (++)	/	/	/	Leptin decreased (from 87.2 [48.6, 132.7] to 39.1 [21.0, 76.4] ng/ml) and adiponectin increased (from 5.6 [4.5, 7.5] to 7.1 [5.5, 8.5] µg/ml). (P<0.05).	Not reported
Hocking et al. [41]	2023	T2D remission in 102/156 participants (66%) after 13 weeks.	/	11.2 % weight loss for ITT population after 13 weeks.	/	/	Two adverse events - hypotension
Anyiam et al. [44]	2023		/	Reduced 14.1 kg	/	/	/
De Freitas et al. [45]	2023	1.4% decrease in HbA1c	Improved FPG	12.3 kg of body weight reduction	Improved lipid profiles	Reduced insulin resistance	/
Khoo et al. [46]	2023	HbA1c was significantly reduced at 12months (6.9±1.5% vs 6.3±0.9%, P =0.003), but not at 24months.	/	The average weight loss at 12 and 24months was 7.1±7.0kg (102.2±20.9kg vs 95.1±18.7kg, P <0.001) and 4.2±7.7kg (102.2±20.9kg vs 98.0±18.2kg, P =0.003), respectively.	/	/	/
Low Glycemic Index MR (n=5)							

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
Stenvers et al. [47]	2014	Did not affect HbA1c (=)	Reduced PPG compared to control (+)	Did not affect weight (=)	Did not affect lipid profile (=)	/	Self-reports of an altered defecation pattern and/or flatulence in eight participants (40 %), nausea in one participant (5 %) and a mild attack of gout in one participant (5 %).
Foster et al. [48]	2013	PCD reduced HbA1c by 0.7%, significantly greater than DSME participants. (++)	Reduced fasting glucose -16.5 mg/dl but not significant. (+)	PCD reduced weight (-7.3kg) sig compared to DSME (-2.2kg) (P<0.0001). (++) BMI reduced significantly (-2.5) (++)	Reduced TG, TC, LDL but not significant. (+) Reduced HDL -0.1 mg/dl (-)	Reduction in intensity of diabetes medication intake by PCD participants Significant greater reduction in BP	No related adverse effects
Boonyavarakul et al. [49]	2018	Reduced HbA1c but not significant – 0.21 ± 0.78 (p = 0.060) (+)	Reduced FPG – 4.02 ± 35.5 but not significant (+)	Weight (–0.78 ± 1.57) and BMI (–0.32 ± 0.63) were significantly reduced. (++)	LDL was significantly decreased (–2.72 ± 22.9 mg/dl) in the MR group compared with the control group. No significant reduction in TC. (+) Increase in TG (8.92 ± 53.3 mg/dl) (-)	/	Not reported
Di et al. [50]	2014	HbA1c of participants taking the breakfast supplement decreased by −0.2% (p=0.004) (++)	Breakfast replacement group had no significant increase in fasting blood glucose (FBG) at week 12 (=)	Reduction of - 0.4kg from baseline (+)	/	/	Not reported
Eliana and Agung Pranoto [51]	2018	/	LMRN reduced glycemic response and incremental area under the curve (+)	/	/	/	Vomiting (one incident) and soft stools (one incident).
Santen et al. [52]	2023	Reduced from 9.60±0.49% at baseline to 7.77±0.47%, (p=0.004)	/	Body weight reduced 7.1% from baseline (p=0.002).	Total Cholesterol – R	/	/
Diabetes Specific Formulas (n=15)							
Belcaro et al. [53]	2009	HbA1c values decreased statistically significantly as compared to baseline from 7.59% to 6.33%. (++)	Treatment group lowered FBG by 30.4%. 145.3 ± 24.5 mg/dL to 101.1 ± 6.2 mg/dL Significant	Weight decreased from 88.5 ±4.4 kg (BMI 26.8 ±4.3 kg/m2) to 81.3 ± 5kg (BMI 24.5 ±4.9 kg/m2) significantly. Significant compared to time and group. (++)	/	/	No adverse effects

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
			compared to time and group. (++)				
Fonda et al. [54]	2010	/	Glucerna has the best profile but still the 2-hour postprandial blood glucose values exceeded the ADA's recommended upper limit for 22% of the subjects (+)	/	/	/	Not reported
Garvey et al. [55]	2006	HbA1c reduced from 6.7 ± 0.1% to 6.3 ± 0.1% (+)	Reduced from 133 ± 3 to 120 ± 2 mg/dL. (+)	Lost 4.8 ± 0.4 kg 38% of subjects lost 5% initial weight (+)	HDL-C increased (3.0±0.9%)	Insulin sensitivity improved, and modest reductions in blood pressure were observed. QOL was improved in all physical and emotional categories assessed by IWQOL, (p=0.006)	Not reported
Sun et al. [56]	2008	HbA1c significantly improved in Intervention vs Reference group (- 0.8 ± 0.1%) (p<0.001) (++)	Mean fasting blood glucose values at 24 weeks were 7.4 ± 0.2 vs 8.9 ± 0.4 mmol/L (p<0.001), Intervention vs Reference, respectively. (++)	Modest reduction of –2.8 ± 0.2% and –3.7 ± 0.3% at each time point for the Intervention Group. (+)	No differences in blood lipids between groups (=)	/	Not reported
Peng et al. [57]	2019	Significantly improved in both the LI+MR and LI groups (++)	Significantly improved in both the LI+MR and LI groups (++)	Both weight and BMI significantly improved in both the LI+MR and LI groups (++)	Significantly improved TG levels (++)	Significantly improved SBP and HOMAIR levels.	Not reported
Chee et al. [58]	2017	Patients in the tDNA groups showed significant lowering of HbA1c (−1.1±0.1%, p<0.001) (++)	FPG reduces signifiantly at tDNAMI group with -1.1 (0.3) mmol/L reduction (p=0.011) (++)	Body weight and BMI reduced significantly in tDNA-MI group with weight loss of 6.9±1.3kg (p<0.001) (++)	HDL and LDL improved significantly (++)	Systolic BP improved significantly (++)	Not reported
Lansink et al. [62]	2011	/	FPG not altered in the diabetes-specific group (from 8.32 ± 0.33 to 8.13 ± 0.33 mmol/L; p = 0.555). (=)	The change in body weight was significantly different between groups (−0.3 ± 0.2 kg in diabetes-specific group and 0.6 ± 0.2 kg in standard group; p = 0.006). (++)	/	/	A low incidence and mild intensity of reported abdominal pain.
Mottalib et al. [63]	2018	HbA1c decreased significantly in groups B (− 0.66%, 95% CI -1.03 to − 0.30) and C (− 0.61%, 95% CI -1.0 to − 0.23) (p < 0.001 for difference among groups). (++)	No change was seen in fasting plasma glucose (=)	Body weight decreased significantly in groups B (− 3.49 kg, 95% CI -4.93 to − 2.05) and C (− 2.93 kg, 95% CI -4.45 to − 1.42) (++)	HDL increased significantly in group C compared to baseline (p < 0.05) (++) TC and LDL did not	/	Not reported

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
					change in any of the groups (=)		
Otto et al. [64]	2009	Mean A1C change at 3 months was – 1.0 ± 1.8 % (p< 0.01) and at 6 months was – 1.2 ± 2.1 % (p< 0.05) (++)	/	Mmean weight change at 3 months was – 3.4 ± 3.3 kg (p<0.001) and at 6 months was – 6.1 ± 14.4 kg (p<0.005) (++)	/	Mean insulin dose change at 3 months was –24.1 ± 38.3 units (p< 0.005) and at 6 months was – 27.7 ± 44.1 units (p< 0.005).	Not reported
Yip et al. [65]	2001	HbA1c decreased from 8.7 ± 1.3% at baseline to 7.9 ± 1.4% (p = 0.0005) at week 12 (++)	Significant reduction of serum glucose over time (p < 0.001). (++)	Reduced 6.10 ± 4.4 kg at week 12 (p = 0.009). (++)	A significant reduction in TC (7.6%) and LDL (12.6%) over time in MR groups (++)	Insulin levels in the MR group were significantly reduced at weeks 4, 8, and 12 compared with baseline.	Not reported
Mottalib et al. [66]	2016	/	Glucose area under the curve (AUC0–240) after GL and UGC was lower than OM (p < 0.001 for both). Insulin positive AUC0–120 after UGC was higher than after OM (p = 0.02). Intake of DSNFs improves PP glucose for 4 h in comparison to oatmeal of similar caloric level.	/	FFA and TG levels were not different between meals. (=)	/	Not reported
Cheskin et al. [67]	2008	At 34 weeks, the PCD group showed a marginally significant reduction (P = .095) in HbA1c by a mean of 0.28% (–2.94%) (++) At 86 weeks, however, HbA1c levels for both groups were no longer statistically different from baseline (=)	At 34 weeks, the PCD group significantly lowered their fasting blood glucose by a mean of 22.2 mg/dL (1.24 mmol/L; 11.3%) from baseline (P = .001) (++) At 86 weeks, both groups had a non significantly lower mean fasting glucose level compared with baseline. (+)	After the 34-week active phase, weight loss among completers was 6.84% (7.3 ± 6.2 kg) on the PCD versus 3.70% (3.7 ± 3.2 kg) on the SD (P = .039). (++) At 86 weeks, completers of both groups maintained significant weight loss. (++)	At 34 weeks, HDL levels were significantly increased in both the PCD (9.1%) (++) At 86 weeks, HDL in the PCD group (up 14.8%, P = .007) remained statistically significant. (++)	At 34 weeks, both groups experienced statistically significant declines in both SBP and DBP. At 86 weeks, the PCD group reduced systolic blood pressure significantly (++)	Not reported

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
Mustad et al. [68]	2020	/	All groups reduced their postprandial glycemic response. (+)	/	/	/	Not reported
Dharmalingam et al. [71]	2022	Mean reduction in HbA1c in PMR group was significant compared to the SOC group (− 0.59 vs. − 0.21%, p = 0.002). (++)	Mean fasting plasma glucose and post-prandial glucose significantly reduced from baseline at week 6 and 12 in each group ($p < 0.05$).	At week 12, the PMR group showed significant reduction in mean body weight (− 2.19 vs. − 0.22 kg; p = 0.001) compared to control.	No significant changes in lipid profile. Slight improvements in TC, TG and HDL. Slight increment in LDL levels	/	No serious adverse events were reported. Six mild adverse effects reported among PMR group:loss of appetite, stomach bloating, peripheral leg edema, burning micturition, and urinary retention.
Zagury et al. [72]	2022	/	The iAUC was lower during the 7-days GTSS period compared to standardized breakfast period (33.3 [15.0-54.0] vs 46.8 [27.3-75.1], p = 0.0376).	/	/	/	No serious adverse events. Four participants (13 %) had mild diarrhea and 3 participants (10 %) had mild nausea
Protein Rich MR (n=10)							
Keogh and Clifton [73]	2012	12 weeks: - 0.49% (P = 0.015) (++) 24 weeks: -0.26% (p=0.5) (+)	Reduced significantly 7.80 ± 1.63 mmol/L to 7.24 ± 1.49 mmol/L at 12 weeks (++)	Reduced weight significantly 102.4 ± 15.4 to 97.45 ± 15.94 kg. (++)	Improved TC, TG and LDL significantly (++)	SBP AND DBP decreased significantly (++). Fat mass/lean mass ratio reduced 10% in MR group	Not reported
Navas-Carretero et al. [74]	2011	/	No significant changes (=)	Modest but significant (p = 0.002) reduction on body weight (1 kg)	No significant changes (-)	/	Not reported
Kempf et al. [76]	2014	HbA1c significantly improved from initially 8.8% (1.4%) to 8.0% (1.2%) (P=0.004) after 4 weeks and further to7.7% (1.1%) (P=0.002) after 8 weeks. Slightly increased to 8.1 % (1.6%) at week 12, but still remained significantly lower than baseline (- 0.8 % (1.4%)), p=0.048.(++)	Fasting blood glucose level reduced by 27.6 (39.6) mg/dL (p=0.027) (++)	All participants significantly reduced their weight from 117.0 (19.7) kg to 115.4 (20.9) kg (P=0.0003) after 4 weeks, and to 112.2 (21.4) kg(P=0.0003) after 8 weeks, reaching a final weight of 107.4 (19.2) kg (P<0.0001) after 12 weeks. (++) Mean reduction of BMI by 2.6 (1.3) (p<0.0001) (++)	Significant reduction in HDL and TG levels (++).	/	Not reported
Kempf et al. [77]	2014	/	/	76% of participants completed the 1-year follow up and maintained	/	In both groups, systolic and diastolic blood pressure were significantly lowered.	Not reported

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
				a significantly lower weight (both p<0.0001). (++) The percentage of participants with greater weight loss was significantly higher in the strict group (p=0.003) (++) In both groups, body mass index (BMI) were significantly lowered. (++)			
Kempf et al. [78]	2015	Significant improvements in HbA1c (-0.9±1.4%; p<0.0001) (++)	/	Significant improvements in weight (-9.9±5.2 kg; p<0.0001) (++)	/	/	Not reported
Martin et al. [79]	2014	Both groups significantly reduced their HbA1c; in the stringent group -0.8 ± 1.4% from 8.6 ± 1.4% to 7.9 ± 1.6% (p<0.001) and in the moderate group -0.5 ± 1.2% from 8.5 ± 1.4% to 7.9 ± 1.2% (p=0.02) (++)	/	Both groups significantly reduced weight (-8.4 ± 6.9 kg; p<0.001 vs. -5.5 ± 5.9 kg; p<0.001) (++)	/	/	Not reported
Li et al. [80]	2005	HbA1C level improved by - 0.49 ± 0.22% for those receiving MR (P<0.05) compared to baseline. (++)	Fasting plasma glucose was significantly reduced in MR group (126.4±4.9 mg/dl) (P<0.0001) at 6 months but not at 12 months. (++)	Percentage weight loss in MR group (4.57±0.81%) was significantly greater (P<0.05) than in IDP group (2.25±0.72%). Significant reduction from baseline in all timepoints. At 12 months -4.35±0.81 kg. (++)	/	High-sensitivity C-reactive protein (hs-CRP) decreased -26.3% (P = 0.019) in MR group compared to -7.06% (P = 0.338) in IDP group at 6 months.	Not reported
Kempf et al. [81]	2017	HbA1c reduction was significantly higher in the TeLiPro group (mean ± SD −1.1 ± 1.2% vs. −0.2 ± 0.8%; P < 0.0001). (++)	More reduction in glucose in TeLiPro compared to control (−21.1 ± 52.4 mg/dL vs −5.3 ± 39.4 mg/dL) (++)	Weight (TeLiPro −6.2 ± 4.6 kg vs. control −1.0 ± 3.4 kg), BMI (−2.1 ± 1.5 kg/m2 vs. −0.3 ± 1.1 kg/m2) (++)	/	Systolic blood pressure (−5.7 ± 15.3 mmHg vs. −1.6 ± 13.8 mmHg), 10-year cardiovascular disease risk, antidiabetes medication, and quality of life and eating behavior (P < 0.01 for all) (++)	Not reported
Shirai et al. [82]	2013	HbA1c started to decrease in both groups at week 4 and significant decreases were maintained until week 24 in both groups (−0.6 ± 1.1%) (p=0.002) (++)	Fasting blood glucose decreased from week 4 and a significant decrease was maintained until week 20 in FD (++)	Weight reduction was greater in FD than in CD (week 24: −3.5 vs −1.4 kg; all p < 0.001) (++)	HDL-cholesterol increased significantly more in FD than in CD (week 24: +2.8 vs. +0.6 mg/dl, p < 0.001) (++)	Insulin and HOMAIR decreased significantly at week 24 at FD (++) In FD, leptin decreased from week 4 to week 12 and increased at weeks 20 and 24. Adiponectin increased gradually in both groups. Lipoprotein lipase mass	Not reported

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
						increased gradually and significantly from week 8 in both groups	
Kerstin et al. [84]	2018	Reduced significantly within groups but not between both of the intervention groups. (++) However, only the S-group showed a clinically relevant improvement in HbA1c of -0.81% [-1.06; -0.55] ($p < 0.001$) after 52 weeks of follow-up.	Reduced significantly within groups but not between both of the intervention groups (++)	Reduced significantly within groups but not between both of the intervention groups. (++)	/	/	Not reported
Low Fat MR (n=1)							
Barbosa-Yañez et al. [86]	2018	Reduced by 0.1% but not significant. (+)	/	Significantly reduced body weight by −5.2 kg ($p< 0.001$) , but not sig between groups. (++)	Significantly improved lipid profile (++)	/	Not reported
MR + Lifestyle Intervention Programme (n=7)							
Delahanty et al. [87]	2020	− 0.6 ± 0.8 % HbA1c at 6 months (+)	/	Percent weight change (95% CI) showed 6-month weight loss of 1.1% (0.2–2.0%) in MNT, the twelve-month weight loss was 2.0% (0.9–3.0%) in MNT.	/	/	Not reported
Wycherley et al. [88]	2008	/	Reduction in glucose level but not significant between group (+)	Overall mean weight loss of 8.8% ($p<0.001$ for time). (++) BMI were reduced by week 12 ($p<0.001$) (++) Magnitude of weight and BMI reduction was not different between treatment groups.	/	/	Not reported
Reynolds et al. [90]	2002	HbA1c reduced significantly by 1.3% for placebo group and 1.1% in RSG group. (both $p<0.05$) (++) All patients reduced -1.2 ± 0.3 % after 24 weeks.	/	All patients reduced -9.2 ± 1.8 kg after week 24. (++)	Modest reduction in total and LDL cholesterol with lifestyle intervention in both groups. (+)	Substantial reduction in WC and blood pressure (++)	Not reported
Hamdy and Carver [91]	2008	HbA 1c decreased significantly, from 7.5% ± 0.14% to 6.6% ± 0.12% ($P < 0.001$). Reduction in HbA	/	Reduce their initial weight by an average of 11.2 ± 0.5 kg (-10.3%, $P < 0.001$) (++)	Lipid profile improved significantly at 12 weeks (++)	/	Not reported

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
		1c correlated significantly with the percentage reduction in BMI (P < 0.05). (++)					
Pi-Sunyer et al. [92]	2009	ILI reduces −0.64 (0.02) % while DSE −0.14 (0.02) % (p<0.001) (++)	ILI reduces −21.5 (0.9) mg/dL while DSE −7.2 (0.9) mg/DL FPG (p<0.001) (++)	ILI group lost an average of 8.6% (standard deviation, 6.9%) of initial body weight compared with 0.7% (4.8%) in the DSE group (p<0.001). (++) 37.8% of ILI participants met the individual weight loss goal (≥10% of initial weight) and 55.2% met the group average goal (≥7%) compared with 3.2% and 7.0% of DSE participants, respectively.	Improved TG and HDL level significantly in ILI group (++)	Greater mean reductions in waist circumference in the ILI than DSE group, with mean decreases of 6.2 (10.2) cm versus 0.5 (8.5) cm: p<0.001.	Not reported
Lean et al. [93]	2018	Reduction of -0.9 (1.4) % HbA1c compared to baseline at 12 months (p<0.0001).	/	Mean bodyweight fell by 10·0 kg in the intervention group (p<0·0001) For participants in the intervention group who engaged with the intervention, weight fell sharply during the total diet replacement phase, by 14·5 kg(95% CI 13·4–15·5), followed by small increases during the food reintroduction phase (1·0 kg [0·3–1·6]) and the weight loss management phase (1·9 kg [1·2–2·5]) (++)	/	Quality of life, as measured by the EuroQol 5 Dimensions visual analogue scale, improved by 7·2 points (SD 21·3) in the intervention group, and decreased by 2·9 points (15·5) in the control group (adjusted difference 6·4 points, 95% CI 2·5–10·3; p=0·0012)	TDR phase reported side effects: 65% participants reported constipation, 57% reported sensitivity to cold and 53% reported headache.
Sattar et al. [94]	2023	Reduced 5.5 mmol/mol from baseline, p=0.20.	Reduced 1.0 mmol/L from baseline, p=0.41.	Reduced 7.2 kg from baseline, p=0.011	Reduced TC but not significant. HDL reduced by -0.02	Reduced waist circumference but not significant.	/
McDiarmid et al. [97]	2021	HbA1c <48 mmol/mol was achieved in 42% of both groups	/	Intention-to-treat analysis at 52 weeks showed percentage weight loss was mean (95% confidence interval) −5.4% (−7.6, −3.1%) for ILED and −6.0% (−7.9, −4.0%) for CLED.	/	/	/

Author, Year	Year	HbA1c	Glucose	Weight (kg)	Lipid Profile	Other Health Status	Adverse effects
Marples et al. [95]	2022	T2DM remission was achieved in 65.7% (n = 23) at 12 months. The mean reduction in HbA1c at 12 months was 15.5 mmol/mol (SD 19.5; p < 0.001)	/	Reduced 14.2 kg (SD 6.5, p < 0.001) and 11.6 kg (SD 8.9, p < 0.001) at 3 and 12 months	Total Cholesterol – R Triglycerides – R** HDL – I LDL – R	/	No serious adverse events were reported; however, side-effects included constipation, diarrhoea, nausea, fatigue and feeling cold.

References

1 **Rothberg AE**, McEwen LN, Kraftson AT, Fowler CE, Herman WH. Very-low-energy diet for type 2 diabetes: an underutilized therapy? *J Diabetes Complications* 2014; **28**: 506-510 [PMID: 24849710 DOI: 10.1016/j.jdiacomp.2014.03.014]

2 **Tatti P**, di Mauro P, Neri M, Pipicelli G, Mussad VA. Effect of a low-calorie high nutritional value formula on weight loss in type 2 diabetes mellitus. *Mediterr J Nutr Metab* 2010; **3**: 65-69 [DOI: 10.1007/s12349-009-0050-7]

3 **Steven S**, Hollingsworth KG, Al-Mrabeh A, Avery L, Aribisala B, Caslake M, Taylor R. Very Low-Calorie Diet and 6 Months of Weight Stability in Type 2 Diabetes: Pathophysiological Changes in Responders and Nonresponders. *Diabetes Care* 2016; **39**: 808-815 [PMID: 27002059 DOI: 10.2337/dc15-1942]

4 **Shantha GP**, Kumar AA, Kahan S, Cheskin LJ. Association between glycosylated hemoglobin and intentional weight loss in overweight and obese patients with type 2 diabetes mellitus: a retrospective cohort study. *Diabetes Educ* 2012; **38**: 417-426 [PMID: 22508341 DOI: 10.1177/0145721712443293]

5 **Astbury NM**, Aveyard P, Nickless A, Hood K, Corfield K, Lowe R, Jebb SA. Doctor Referral of Overweight People to Low Energy total diet replacement Treatment (DROPLET): pragmatic randomised controlled trial. *BMJ* 2018; **362**: k3760 [PMID: 30257983 DOI: 10.1136/bmj.k3760]

6 **Baker ST**, Jerums G, Prendergast LA, Panagiotopoulos S, Strauss BJ, Proietto J. Less fat reduction per unit weight loss in type 2 diabetic compared with nondiabetic obese individuals completing a very-low-calorie diet program. *Metabolism* 2012; **61**: 873-882 [PMID: 22146094 DOI: 10.1016/j.metabol.2011.10.017]

7 Bishay R. TWO BIRDS - Intensive lifestyle and medication to help improve diabetes and fatty liver disease through weight loss. https://trialsearchwhoint/Trial2aspx?TrialID=ACTRN12619000931178. 2019.

8 **Bhatt AA**, Choudhari PK, Mahajan RR, Sayyad MG, Pratyush DD, Hasan I, Javherani RS, Bothale MM, Purandare VB, Unnikrishnan AG. Effect of a Low-Calorie Diet on

Restoration of Normoglycemia in Obese subjects with Type 2 Diabetes. *Indian J Endocrinol Metab* 2017; **21**: 776-780 [PMID: 28989891 DOI: 10.4103/ijem.IJEM_206_17]

9 **Berk KA**, Vongpromek R, Jiang M, Schneider WJ, Timman R, Verhoeven AJ, Bujo H, Sijbrands EJ, Mulder MT. Levels of the soluble LDL receptor-relative LR11 decrease in overweight individuals with type 2 diabetes upon diet-induced weight loss. *Atherosclerosis* 2016; **254**: 67-72 [PMID: 27697674 DOI: 10.1016/j.atherosclerosis.2016.09.066]

10 **Shiau JY**, So DYF, Dent RR. Effects on Diabetes Medications, Weight and Glycated Hemoglobin Among Adult Patients With Obesity and Type 2 Diabetes: 6-Month Observations From a Full Meal Replacement, Low-Calorie Diet Weight Management Program. *Can J Diabetes* 2018; **42**: 56-60 [PMID: 28600119 DOI: 10.1016/j.jcjd.2017.03.006]

11 **Cinkajzlová A**, Lacinová Z, Kloučková J, Kaválková P, Trachta P, Kosák M, Krátký J, Kasalický M, DoleŽalová K, Mráz M, Haluzík M. An alternatively activated macrophage marker CD163 in severely obese patients: the influence of very low-calorie diet and bariatric surgery. *Physiol Res* 2017; **66**: 641-652 [PMID: 28406702 DOI: 10.33549/physiolres.933522]

12 **Taheri S**, Chagoury O, Zaghloul H, Elhadad S, Ahmed SH, Omar O, Payra S, Ahmed S, El Khatib N, Amona RA, El Nahas K, Bolton M, Chaar H, Suleiman N, Jayyousi A, Zirie M, Janahi I, Elhag W, Alnaama A, Zainel A, Hassan D, Cable T, Charlson M, Wells M, Al-Hamaq A, Al-Abdulla S, Abou-Samra AB. Diabetes Intervention Accentuating Diet and Enhancing Metabolism (DIADEM-I): a randomised controlled trial to examine the impact of an intensive lifestyle intervention consisting of a low-energy diet and physical activity on body weight and metabolism in early type 2 diabetes mellitus: study protocol for a randomized controlled trial. *Trials* 2018; **19**: 284 [PMID: 29784059 DOI: 10.1186/s13063-018-2660-1]

13 **Harder H**, Dinesen B, Astrup A. The effect of a rapid weight loss on lipid profile and glycemic control in obese type 2 diabetic patients. *Int J Obes Relat Metab Disord* 2004; **28**: 180-182 [PMID: 14610532 DOI: 10.1038/sj.ijo.0802529]

14 **Friedman AN**, Chambers M, Kamendulis LM, Temmerman J. Short-term changes after a weight reduction intervention in advanced diabetic nephropathy. *Clin J Am Soc Nephrol* 2013; **8**: 1892-1898 [PMID: 23929927 DOI: 10.2215/CJN.04010413]

15 **Lean M**, Leslie W. Study to determine the feasibility and acceptability of an intensive weight management programme, to achieve remission of diabetes, in patients of South Asian Ethnicity. *http://isrctn.com/* [DOI: 10.1186/isrctn10720065]

16 Wong TW, Ching KM, Chan WS, Lee H, Wong SC, S A, et al. A 24-week structured multidisciplinary weight reduction program in overweight type 2 diabetic patients in a hospital outpatient setting: clinical diabetes. 2016;7:47-8.

17 **Leader NJ**, Ryan L, Molyneaux L, Yue DK. How best to use partial meal replacement in managing overweight or obese patients with poorly controlled type 2 diabetes. *Obesity (Silver Spring)* 2013; **21**: 251-253 [PMID: 23404963 DOI: 10.1002/oby.20057]

18 Overl, J, Griffiths C, Gauld A, Gibson A, Franklin J, et al. Intermittent Fasting vs. Continuous energy restriction: a pilot study in people with type 2 diabetes and overweight and obesity. 2017;66:A202-.

19 **Gulsin GS**, Swarbrick DJ, Athithan L, Brady EM, Henson J, Baldry E, Argyridou S, Jaicim NB, Squire G, Walters Y, Marsh AM, McAdam J, Parke KS, Biglands JD, Yates T, Khunti K, Davies MJ, McCann GP. Effects of Low-Energy Diet or Exercise on Cardiovascular Function in Working-Age Adults With Type 2 Diabetes: A Prospective, Randomized, Open-Label, Blinded End Point Trial. *Diabetes Care* 2020; **43**: 1300-1310 [PMID: 32220917 DOI: 10.2337/dc20-0129]

20 **Farrer O**, Golley R. Feasibility study for efficacy of group weight management programmes achieving therapeutic weight loss in people with type 2 diabetes. *Nutrition & Dietetics* 2014; **71**: 16-21 [DOI: 10.1111/1747-0080.12048]

21 **Sumithran P**, Proietto J. Safe year-long use of a very-low-calorie diet for the treatment of severe obesity. *Med J Aust* 2008; **188**: 366-368 [PMID: 18341463 DOI: 10.5694/j.1326-5377.2008.tb01657.x]

22 **Rolland C**, Lula S, Jenner C, Dyson L, Macdonald I, Johnston KL, Broom I. Weight loss for individuals with type 2 diabetes following a very-low-calorie diet in a community-

based setting with trained facilitators for 12 weeks. *Clin Obes* 2013; **3**: 150-157 [PMID: 25586630 DOI: 10.1111/cob.12029]

23 **Dhindsa P**, Scott AR, Donnelly R. Metabolic and cardiovascular effects of very-low-calorie diet therapy in obese patients with Type 2 diabetes in secondary failure: outcomes after 1 year. *Diabet Med* 2003; **20**: 319-324 [PMID: 12675647 DOI: 10.1046/j.1464-5491.2003.00937.x]

24 **Khoo J**, Piantadosi C, Duncan R, Worthley SG, Jenkins A, Noakes M, Worthley MI, Lange K, Wittert GA. Comparing effects of a low-energy diet and a high-protein low-fat diet on sexual and endothelial function, urinary tract symptoms, and inflammation in obese diabetic men. *J Sex Med* 2011; **8**: 2868-2875 [PMID: 21819545 DOI: 10.1111/j.1743-6109.2011.02417.x]

25 **Moriconi E**, Camajani E, Fabbri A, Lenzi A, Caprio M. Very-Low-Calorie Ketogenic Diet as a Safe and Valuable Tool for Long-Term Glycemic Management in Patients with Obesity and Type 2 Diabetes. *Nutrients* 2021; **13** [PMID: 33652834 DOI: 10.3390/nu13030758]

26 **Tang F**, Lin X. Effects of Fasting-Mimicking Diet and Specific Meal Replacement Foods on Blood Glucose Control in Patients with Type 2 Diabetes: A Randomized Controlled Trial. *Oxid Med Cell Longev* 2020; **2020**: 6615295 [PMID: 33376581 DOI: 10.1155/2020/6615295]

27 **Maher M**, Rafey MF, Griffin H, Cunningham K, Finucane FM. Utilising a milk-based meal replacement programme in a bariatric patient with poorly controlled type 2 diabetes mellitus. *Endocrinol Diabetes Metab Case Rep* 2019; **2019** [PMID: 30959473 DOI: 10.1530/EDM-19-0008]

28 **Nori Janosz KE**, Koenig Berris KA, Leff C, Miller WM, Yanez J, Myers S, Vial C, Vanderlinden M, Franklin BA, Mccullough PA. Clinical Resolution of Type 2 Diabetes with Reduction in Body Mass Index Using Meal Replacement Based Weight Loss. *Vascular Disease Prevention* 2008; **5**: 17-23 [DOI: 10.2174/156727008783503134]

29 **Storck LJ**, Meffert PJ, Rausch J, Gärtner S, Aghdassi AA, Kühn JP, Kraft M, Pietzner M, Lerch MM, Steveling A. Efficiency of a 15-Week Weight-Loss Program, Including a

Low-Calorie Formula Diet, on Glycemic Control in Patients with Type 2 Diabetes Mellitus and Overweight or Obesity. *Obes Facts* 2021; **14**: 1-11 [PMID: 33601371 DOI: 10.1159/000511453]

30 **Schwasinger-Schmidt TE**, Elhomsy G, Paull-Forney BG. Impact of a Community-Based Weight Loss Program on Renal Function. *Cureus* 2020; **12**: e8101 [PMID: 32542156 DOI: 10.7759/cureus.8101]

31 **Steven S**, Taylor R. Restoring normoglycaemia by use of a very low calorie diet in long- and short-duration Type 2 diabetes. *Diabet Med* 2015; **32**: 1149-1155 [PMID: 25683066 DOI: 10.1111/dme.12722]

32 **Redmon JB**, Raatz SK, Reck KP, Swanson JE, Kwong CA, Fan Q, Thomas W, Bantle JP. One-year outcome of a combination of weight loss therapies for subjects with type 2 diabetes: a randomized trial. *Diabetes Care* 2003; **26**: 2505-2511 [PMID: 12941710 DOI: 10.2337/diacare.26.9.2505]

33 **Lips MA**, de Groot GH, van Klinken JB, Aarts E, Berends FJ, Janssen IM, Van Ramshorst B, Van Wagensveld BA, Swank DJ, Van Dielen F, Willems van Dijk K, Pijl H. Calorie restriction is a major determinant of the short-term metabolic effects of gastric bypass surgery in obese type 2 diabetic patients. *Clin Endocrinol (Oxf)* 2014; **80**: 834-842 [PMID: 23711328 DOI: 10.1111/cen.12254]

34 Elizabeth O Beale M. A Trial of Meal Replacement at a Community Diabetes Clinic Serving a Low Socioeconomic Hispanic Population. 2012.

35 Abi-Chahine T, Chatterjee S, Cooper C, Willis T, Morais M, Hadfield W. Community-based pilot study of type 2 diabetes remission through weight loss achieved by total diet replacement based on direct trial. Diabetic Medicine. 2021;38.

36 **Rafey MF**, Abdalgwad R, O'Shea PM, Foy S, Claffey B, Davenport C, O'Keeffe DT, Finucane FM. Changes in the Leptin to Adiponectin Ratio Are Proportional to Weight Loss After Meal Replacement in Adults With Severe Obesity. *Front Nutr* 2022; **9**: 845574 [PMID: 35662920 DOI: 10.3389/fnut.2022.845574]

37 Reynolds A. A primary care-led weight management intervention for adults with type 2 diabetes and obesity: diRECT to Aotearoa New Zealand [Internet]. 2022. Available from: https://trialsearch.who.int/Trial2.aspx?TrialID=ACTRN12622000151730.

38 **Scragg J**, Morris E, Wane S, Noreik M, Jerome D, Yu LM, Galal U, Dyson P, Tan GD, Fox R, Breeze P, Thomas C, Jebb SA, Aveyard P. Dietary Approaches to the Management Of type 2 Diabetes (DIAMOND) in primary care: A protocol for a cluster randomised trial. *Contemp Clin Trials* 2023; **129**: 107199 [PMID: 37094737 DOI: 10.1016/j.cct.2023.107199]

39 **Tsompanaki E**, Aveyard P, Park RJ, Koutoukidis DA. The Impact of Low-Energy Total Diet Replacement with Behavioural Support for Remission of Type 2 Diabetes on Disordered Eating (Ariadne): Protocol for a Non-Inferiority Randomised Controlled Trial [DOI: 10.2139/ssrn.4611889]

40 Shirmann F. SAFE-LCD A Randomised Controlled Trial for Insulin-treated Adults Living With Type 2 Diabetes [Internet]. 2023. Available from: https://clinicaltrials.gov/study/NCT06119204.

41 **Hocking SL**, Markovic TP, Lee CMY, Picone TJ, Gudorf KE, Colagiuri S. Intensive Lifestyle Intervention for Remission of Early Type 2 Diabetes in Primary Care in Australia: DiRECT-Aus. *Diabetes Care* 2024; **47**: 66-70 [PMID: 37840461 DOI: 10.2337/dc23-0781]

42 Ekberg NR. Normalized Glucose Levels in Type 2 Diabetes With Carbohydrate or Caloric Restriction [Internet]. ClinicalTrials.gov. 2023. Available from: https://clinicaltrials.gov/study/NCT05801614.

43 Otten J. The eHealth Diabetes Remission Trial [Internet]. 2022. Available from: https://clinicaltrials.gov/study/NCT05491005.

44 **Anyiam O**, Phillips BE, Wilkinson DJ, Smith K, Atherton PJ, Idris IR. 278-LB: The Effect of Combining Very-Low-Calorie Diet with Semaglutide on Beta-Cell Function in Individuals with Type 2 Diabetes. *Diabetes* 2023; **72** [DOI: 10.2337/db23-278-lb]

45 **De Freitas MF**, Neidert A, Nay C, Chenevert T, Oral E, Rothberg A. RF24 | PSUN126 A Very-Low Calorie Diet Can Reduce Insulin Resistance and Cause Remission of Diabetes Mellitus and Hypertriglyceridemia in a Patient With Familial Partial

Lipodystrophy Type 2. *Journal of the Endocrine Society* 2022; **6**: A34-A34 [DOI: 10.1210/jendso/bvac150.071]

46 **Khoo CL**, Chimoriya R, Simmons D, Piya MK. Partial meal replacement for people with type 2 diabetes: 2-year outcomes from an Australian general practice. *Aust J Prim Health* 2023; **29**: 74-80 [PMID: 36318919 DOI: 10.1071/PY22180]

47 **Stenvers DJ**, Schouten LJ, Jurgens J, Endert E, Kalsbeek A, Fliers E, Bisschop PH. Breakfast replacement with a low-glycaemic response liquid formula in patients with type 2 diabetes: a randomised clinical trial. *Br J Nutr* 2014; **112**: 504-512 [PMID: 25091284 DOI: 10.1017/S0007114514001123]

48 **Foster GD**, Wadden TA, Lagrotte CA, Vander Veur SS, Hesson LA, Homko CJ, Maschak-Carey BJ, Barbor NR, Bailer B, Diewald L, Komaroff E, Herring SJ, Vetter ML. A randomized comparison of a commercially available portion-controlled weight-loss intervention with a diabetes self-management education program. *Nutr Diabetes* 2013; **3**: e63 [PMID: 23507967 DOI: 10.1038/nutd.2013.3]

49 **Boonyavarakul A**, Leelawattana R, Pongchaiyakul C, Buranapin S, Phanachet P, Pramyothin P. Effects of meal replacement therapy on metabolic outcomes in Thai patients with type 2 diabetes: A randomized controlled trial. *Nutr Health* 2018; **24**: 261-268 [PMID: 30270717 DOI: 10.1177/0260106018800074]

50 **Li D**, Zhang P, Guo H, Ling W. Taking a low glycemic index multi-nutrient supplement as breakfast improves glycemic control in patients with type 2 diabetes mellitus: a randomized controlled trial. *Nutrients* 2014; **6**: 5740-5755 [PMID: 25514391 DOI: 10.3390/nu6125740]

51 **Eliana F**, Pranoto BA. A randomized controlled clinical trial of carbohydrate mix-fortified nutrition in type 2 diabetes mellitus patients. *Med J Indones* 2020; **29**: 275-82 [DOI: 10.13181/mji.oa.203398]

52 **Santen RJ**. Patients with diabetes in rural underserved areas. *Open Access Government* 2023; **40**: 118-119 [DOI: 10.56367/oag-040-10840]

53 **Belcaro G**, Cesarone M, Silvia E, Ledda A, Stuard S, G V, Dougall M, Cornelli U, Hastings C, Schönlau F. Daily consumption of Reliv Glucaffect for 8 weeks significantly

lowered blood glucose and body weight in 50 subjects. *Phytother Res* 2009; **23**: 1673-1677 [PMID: 19405040 DOI: 10.1002/ptr.2793]

54 **Fonda SJ**, Jain A, Vigersky RA. A head-to-head comparison of the postprandial effects of 3 meal replacement beverages among people with type 2 diabetes. *Diabetes Educ* 2010; **36**: 793-800 [PMID: 20876307 DOI: 10.1177/0145721710378537]

55 Garvey WT, Baumgartner CJ, Fern, es JK, Fernstrom MH, Lausch MJ, et al. A Diabetes Management Program Using Diabetes-Specific Meal Replacements and Snack Bars Improves Weight Loss, Metabolic Parameters, and Quality of Life (QOL): 2577-PO. DIABETES. 2006;55:A596-A.

56 Sun JQ, Wang YF, Chen XF, Chen YQ, Feng Y, Zhang XY, et al. An integrated intervention program to control diabetes in overweight Chinese women and men with type 2 diabetes. Asia Pac J Clin Nutr. 2008;17(3):514-24.

57 **Peng J**, Lu J, Ma X, Ying L, Lu W, Zhu W, Bao Y, Zhou J. Breakfast replacement with a liquid formula improves glycaemic variability in patients with type 2 diabetes: a randomised clinical trial. *Br J Nutr* 2019; **121**: 560-566 [PMID: 30526707 DOI: 10.1017/S0007114518003628]

58 **Chee WSS**, Gilcharan Singh HK, Hamdy O, Mechanick JI, Lee VKM, Barua A, Mohd Ali SZ, Hussein Z. Structured lifestyle intervention based on a trans-cultural diabetes-specific nutrition algorithm (tDNA) in individuals with type 2 diabetes: a randomized controlled trial. *BMJ Open Diabetes Res Care* 2017; **5**: e000384 [PMID: 29435347 DOI: 10.1136/bmjdrc-2016-000384]

59 Patel N. Evaluate Partial Meal Replacement with Prohance D (Nutraceutical Product) in type II Diabetic Population. 2019.

60 Hwu C-M. A Study to Evaluate the Postprandial Metabolic Response After Use of Glucerna SR in Obese Type 2 Diabetes. https://clinicaltrialsgov/show/NCT00631774. 2008.

61 Bao Y. The Efficacy of Glucerna SR in Chinese Drug-naïve Subjects With Type 2 Diabetes. Asia Pacific journal of clinical nutrition. 2014.

62 **Lansink M**, van Laere KM, Vendrig L, Rutten GE. Lower postprandial glucose responses at baseline and after 4 weeks use of a diabetes-specific formula in diabetes type 2 patients. *Diabetes Res Clin Pract* 2011; **93**: 421-429 [PMID: 21680040 DOI: 10.1016/j.diabres.2011.05.019]

63 **Mottalib A**, Salsberg V, Mohd-Yusof BN, Mohamed W, Carolan P, Pober DM, Mitri J, Hamdy O. Effects of nutrition therapy on HbA1c and cardiovascular disease risk factors in overweight and obese patients with type 2 diabetes. *Nutr J* 2018; **17**: 42 [PMID: 29626933 DOI: 10.1186/s12937-018-0351-0]

64 **Otto R**, Mullan Y, Gerstein H. The effect of partial meal replacement therapy on weight loss and glycaemic control in obese individuals with type 2 diabetes. *Canadian Journal of Diabetes* 2009; **33**: 269 [DOI: 10.1016/s1499-2671(09)33216-5]

65 **Yip I**, Go VL, DeShields S, Saltsman P, Bellman M, Thames G, Murray S, Wang HJ, Elashoff R, Heber D. Liquid meal replacements and glycemic control in obese type 2 diabetes patients. *Obes Res* 2001; **9 Suppl 4**: 341S-347S [PMID: 11707563 DOI: 10.1038/oby.2001.140]

66 **Mottalib A**, Mohd-Yusof BN, Shehabeldin M, Pober DM, Mitri J, Hamdy O. Impact of Diabetes-Specific Nutritional Formulas versus Oatmeal on Postprandial Glucose, Insulin, GLP-1 and Postprandial Lipidemia. *Nutrients* 2016; **8** [PMID: 27455318 DOI: 10.3390/nu8070443]

67 **Cheskin LJ**, Mitchell AM, Jhaveri AD, Mitola AH, Davis LM, Lewis RA, Yep MA, Lycan TW. Efficacy of meal replacements versus a standard food-based diet for weight loss in type 2 diabetes: a controlled clinical trial. *Diabetes Educ* 2008; **34**: 118-127 [PMID: 18267998 DOI: 10.1177/0145721707312463]

68 **Mustad VA**, Hegazi RA, Hustead DS, Budiman ES, Rueda R, Maki K, Powers M, Mechanick JI, Bergenstal RM, Hamdy O. Use of a diabetes-specific nutritional shake to replace a daily breakfast and afternoon snack improves glycemic responses assessed by continuous glucose monitoring in people with type 2 diabetes: a randomized clinical pilot study. *BMJ Open Diabetes Res Care* 2020; **8** [PMID: 32718934 DOI: 10.1136/bmjdrc-2020-001258]

69 **Lew LC**, Mat Ludin AF, Shahar S, Abdul Manaf Z, Mohd Tohit N. Efficacy and Sustainability of Diabetes-Specific Meal Replacement on Obese and Overweight Type-2 Diabetes Mellitus Patients: Study Approaches for a Randomised Controlled Trial and Impact of COVID-19 on Trial Progress. *Int J Environ Res Public Health* 2022; **19** [PMID: 35409872 DOI: 10.3390/ijerph19074188]

70 Wichansawakun S. Efficacy of using diabetic specific formula as a meal replacement to control blood sugar level.2023. Available from: https://www.cochranelibrary.com/central/doi/10.1002/central/CN-02521734/full.

71 **Dharmalingam M**, Das R, Jain S, Gupta S, Gupta M, Kudrigikar V, Bachani D, Mehta S, Joglekar S. Impact of Partial Meal Replacement on Glycemic Levels and Body Weight in Indian Patients with Type 2 Diabetes (PRIDE): A Randomized Controlled Study. *Diabetes Ther* 2022; **13**: 1599-1619 [PMID: 35834107 DOI: 10.1007/s13300-022-01294-0]

72 **Zagury RL**, Lacativa P, Gregório LH, Rosenfeld VAS, Campos LF, Pinheiro RAC, Ferreira da Costa S, Russo LAT. Randomized clinical trial to evaluate the effect on postprandial glycemia of Nutren Control®, a glycemia-targeted specialized supplement, compared to standardized breakfast in patients with type-2 diabetes: the CONTROL DIABETES study. *Nutr Hosp* 2023; **40**: 41-48 [PMID: 36602126 DOI: 10.20960/nh.04204]

73 **Keogh JB**, Clifton PM. Meal replacements for weight loss in type 2 diabetes in a community setting. *J Nutr Metab* 2012; **2012**: 918571 [PMID: 23091707 DOI: 10.1155/2012/918571]

74 **Navas-Carretero S**, Abete I, Zulet MA, Martínez JA. Chronologically scheduled snacking with high-protein products within the habitual diet in type-2 diabetes patients leads to a fat mass loss: a longitudinal study. *Nutr J* 2011; **10**: 74 [PMID: 21756320 DOI: 10.1186/1475-2891-10-74]

75 Manjunath R. Effect of soya protein powder "ALMASED" on Diabetic patients. 2011.

76 **Kempf K**, Schloot NC, Gärtner B, Keil R, Schadewaldt P, Martin S. Meal replacement reduces insulin requirement, HbA1c and weight long-term in type 2 diabetes patients with >100 U insulin per day. *J Hum Nutr Diet* 2014; **27 Suppl 2**: 21-27 [PMID: 23909831 DOI: 10.1111/jhn.12145]

77 Kempf K, Gärtner B, Keil R, Ullmann S, Martin S. Long-term reduction of weight and antidiabetic medication by protein-rich meal replacement in type 2 diabetes patients-a randomized, controlled trial. 2014;63:A386-.
78 Kempf K, Niedermeier K, Gärtner B, Keil R, Martin S. Elevated fasting insulin levels at baseline predict a poorer hba1c outcome long-term after protein-rich meal replacement in poorly controlled type 2 diabetes patients-a randomized controlled trial. DIABETES. 2015;64:A211-.
79 Martin S, Gärtner B, Keil R, Kempf K. Protein-rich meal replacement significantly reduces HbA1c, weight and antidiabetic medication in type 2 diabetes patients: a randomized controlled trial. 2013;62:A194-.
80 **Li Z**, Hong K, Saltsman P, DeShields S, Bellman M, Thames G, Liu Y, Wang HJ, Elashoff R, Heber D. Long-term efficacy of soy-based meal replacements vs an individualized diet plan in obese type II DM patients: relative effects on weight loss, metabolic parameters, and C-reactive protein. *Eur J Clin Nutr* 2005; **59**: 411-418 [PMID: 15674301 DOI: 10.1038/sj.ejcn.1602089]
81 **Kempf K**, Altpeter B, Berger J, Reuß O, Fuchs M, Schneider M, Gärtner B, Niedermeier K, Martin S. Efficacy of the Telemedical Lifestyle intervention Program TeLiPro in Advanced Stages of Type 2 Diabetes: A Randomized Controlled Trial. *Diabetes Care* 2017; **40**: 863-871 [PMID: 28500214 DOI: 10.2337/dc17-0303]
82 **Shirai K**, Saiki A, Oikawa S, Teramoto T, Yamada N, Ishibashi S, Tada N, Miyazaki S, Inoue I, Murano S, Sakane N, Satoh-Asahara N, Bujo H, Miyashita Y, Saito Y. The effects of partial use of formula diet on weight reduction and metabolic variables in obese type 2 diabetic patients--multicenter trial. *Obes Res Clin Pract* 2013; **7**: e43-e54 [PMID: 24331681 DOI: 10.1016/j.orcp.2012.03.002]
83 **Durrer C**, McKelvey S, Singer J, Batterham AM, Johnson JD, Wortman J, Little JP. Pharmacist-led therapeutic carbohydrate restriction as a treatment strategy for type 2 diabetes: the Pharm-TCR randomized controlled trial protocol. *Trials* 2019; **20**: 781 [PMID: 31881991 DOI: 10.1186/s13063-019-3873-7]

84 **Kempf K**, Röhling M, Niedermeier K, Gärtner B, Martin S. Individualized Meal Replacement Therapy Improves Clinically Relevant Long-Term Glycemic Control in Poorly Controlled Type 2 Diabetes Patients. *Nutrients* 2018; **10** [PMID: 30081574 DOI: 10.3390/nu10081022]

85 **Papakonstantinou E**, Triantafillidou D, Panagiotakos DB, Koutsovasilis A, Saliaris M, Manolis A, Melidonis A, Zampelas A. A high-protein low-fat diet is more effective in improving blood pressure and triglycerides in calorie-restricted obese individuals with newly diagnosed type 2 diabetes. *Eur J Clin Nutr* 2010; **64**: 595-602 [PMID: 20216558 DOI: 10.1038/ejcn.2010.29]

86 **Barbosa-Yañez RL**, Dambeck U, Li L, Machann J, Kabisch S, Pfeiffer AFH. Acute Endothelial Benefits of Fat Restriction over Carbohydrate Restriction in Type 2 Diabetes Mellitus: Beyond Carbs and Fats. *Nutrients* 2018; **10** [PMID: 30513768 DOI: 10.3390/nu10121859]

87 **Delahanty LM**, Levy DE, Chang Y, Porneala BC, Goldman V, McCarthy J, Bissett L, Rodriguez AR, Chase B, LaRocca R, Wheeler A, Wexler DJ. Effectiveness of Lifestyle Intervention for Type 2 Diabetes in Primary Care: the REAL HEALTH-Diabetes Randomized Clinical Trial. *J Gen Intern Med* 2020; **35**: 2637-2646 [PMID: 31965526 DOI: 10.1007/s11606-019-05629-9]

88 **Wycherley TP**, Brinkworth GD, Noakes M, Buckley JD, Clifton PM. Effect of caloric restriction with and without exercise training on oxidative stress and endothelial function in obese subjects with type 2 diabetes. *Diabetes Obes Metab* 2008; **10**: 1062-1073 [PMID: 18435772 DOI: 10.1111/j.1463-1326.2008.00863.x]

89 **McDiarmid S**, Harvie M, Johnson R, Vyas A, Aglan A, Moran J, Ruane H, Hulme A, Sellers K, Issa B. Intermittent Versus Continuous Low-Energy Diet in Patients With Type 2 Diabetes: Protocol for a Pilot Randomized Controlled Trial. *JMIR Res Protoc* 2021; **10**: e21116 [PMID: 33739297 DOI: 10.2196/21116]

90 **Reynolds LR**, Konz EC, Frederich RC, Anderson JW. Rosiglitazone amplifies the benefits of lifestyle intervention measures in long-standing type 2 diabetes mellitus.

Diabetes Obes Metab 2002; **4**: 270-275 [PMID: 12099976 DOI: 10.1046/j.1463-1326.2002.00207.x]

91 **Hamdy O**, Carver C. The Why WAIT program: improving clinical outcomes through weight management in type 2 diabetes. *Curr Diab Rep* 2008; **8**: 413-420 [PMID: 18778592 DOI: 10.1007/s11892-008-0071-5]

92 **Look AHEAD Research Group**, Pi-Sunyer X, Blackburn G, Brancati FL, Bray GA, Bright R, Clark JM, Curtis JM, Espeland MA, Foreyt JP, Graves K, Haffner SM, Harrison B, Hill JO, Horton ES, Jakicic J, Jeffery RW, Johnson KC, Kahn S, Kelley DE, Kitabchi AE, Knowler WC, Lewis CE, Maschak-Carey BJ, Montgomery B, Nathan DM, Patricio J, Peters A, Redmon JB, Reeves RS, Ryan DH, Safford M, Van Dorsten B, Wadden TA, Wagenknecht L, Wesche-Thobaben J, Wing RR, Yanovski SZ. Reduction in weight and cardiovascular disease risk factors in individuals with type 2 diabetes: one-year results of the look AHEAD trial. *Diabetes Care* 2007; **30**: 1374-1383 [PMID: 17363746 DOI: 10.2337/dc07-0048]

93 **Lean ME**, Leslie WS, Barnes AC, Brosnahan N, Thom G, McCombie L, Peters C, Zhyzhneuskaya S, Al-Mrabeh A, Hollingsworth KG, Rodrigues AM, Rehackova L, Adamson AJ, Sniehotta FF, Mathers JC, Ross HM, McIlvenna Y, Stefanetti R, Trenell M, Welsh P, Kean S, Ford I, McConnachie A, Sattar N, Taylor R. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. *Lancet* 2018; **391**: 541-551 [PMID: 29221645 DOI: 10.1016/S0140-6736(17)33102-1]

94 **Sattar N**, Welsh P, Leslie WS, Thom G, McCombie L, Brosnahan N, Richardson J, Gill JMR, Crawford L, Lean MEJ. Dietary weight-management for type 2 diabetes remissions in South Asians: the South Asian diabetes remission randomised trial for proof-of-concept and feasibility (STANDby). *Lancet Reg Health Southeast Asia* 2023; **9**: 100111 [PMID: 36777452 DOI: 10.1016/j.lansea.2022.100111]

95 **Marples O**, Resca L, Plavska J, Hassan S, Mistry V, Mallik R, Brown A. Real-World Data of a Group-Based Formula Low Energy Diet Programme in Achieving Type 2

Diabetes Remission and Weight Loss in an Ethnically Diverse Population in the UK: A Service Evaluation. *Nutrients* 2022; **14** [PMID: 35956322 DOI: 10.3390/nu14153146]

96 **Dasgupta K**, Boulé N, Henson J, Chevalier S, Redman E, Chan D, McCarthy M, Champagne J, Arsenyadis F, Rees J, Da Costa D, Gregg E, Yeung R, Hadjiconstantinou M, Dattani A, Friedrich MG, Khunti K, Rahme E, Fortier I, Prado CM, Sherman M, Thompson RB, Davies MJ, McCann GP, Yates T. Remission of type 2 diabetes and improved diastolic function by combining structured exercise with meal replacement and food reintroduction among young adults: the RESET for REMISSION randomised controlled trial protocol. *BMJ Open* 2022; **12**: e063888 [PMID: 36130753 DOI: 10.1136/bmjopen-2022-063888]

97 **McDiarmid S**, Harvie M, Johnson R, Vyas A, Aglan A, Moran J, Ruane H, Hulme A, Sellers K, Issa BG. Manchester Intermittent versus Daily Diet App Study (MIDDAS): A pilot randomized controlled trial in patients with type 2 diabetes. *Diabetes Obes Metab* 2022; **24**: 432-441 [PMID: 34726317 DOI: 10.1111/dom.14592]