RESEARCH ARTICLE

Type 2 diabetes remission and its predictors in an Indian cohort: A retrospective analysis of an intensive lifestyle intervention program

Pramod Tripathi[1,2], Nidhi Kadam [1*], Thejas Kathrikolly[1], Diptika Tiwari [1], Anagha Vyawahare[1], Baby Sharma[1], Malhar Ganla[2], Banshi Saboo[3]

1 Department of Research, Freedom from Diabetes Research Foundation, Pune, Maharashtra, India, 2 Department of Management and Exercise Science, Freedom from Diabetes Clinic, Pune, Maharashtra, India, 3 Department of Medicine, Dia Care - Diabetes Care and Hormone Clinic, Ahmedabad, Gujarat, India

* research@freedomfromdiabetes.org

Abstract

Predictors of type 2 diabetes (T2D) remission following intensive lifestyle intervention (ILI) are poorly characterized, especially in high-risk populations, such as India. This study aimed to identify the key predictors of T2D remission after an ILI in an Indian population. This retrospective analysis included 2384 patients with T2D (age 30–75 years; body mass index (BMI) ≥23 kg/m² enrolled in an online one-year ILI program at the Freedom from Diabetes Clinic, India, between May 2021 and August 2023. The intervention included personalized plant-based diet, physical activity, stress management, and medical support. Remission was defined as maintaining glycated hemoglobin (HbA1c) < 48 mmol/mol (6.5%) for ≥3 months without glucose-lowering medications. Anthropometric and biochemical data were extracted from clinical records. Predictors were assessed using logistic regression analysis. Post- intervention, 744 patients (31.2%) achieved remission The remission group showed significantly greater improvements in weight (−8.5% vs. −5.2%), BMI (−8.6% vs. −5.2%), HbA1c (−15.3% vs. −12.4%), fasting insulin (−26.6% vs. −11.4%), and homeostatic model assessment of insulin resistance (HOMA-IR) (−37.3% vs. −19.7%), than the non-remission group (p<0.05). The predictors of remission included age (≤50 years), higher BMI (≥25 kg/m²), drug-naïve status, shorter disease duration (≤6 years), juice fasting, baseline HbA1c<7%, weight loss >10%, and post-intervention HOMA-IR<2.5 (p <0.05). Our findings demonstrate that a significant proportion of individuals with T2D can achieve remission through a comprehensive culturally adapted lifestyle program. The identification of both baseline and post-intervention predictors underscores the importance of early, personalized, and holistic care in diabetes management.

Introduction

Type 2 diabetes (T2D) is a global health concern, primarily driven by lifestyle factors and comorbidities. The International Diabetes Federation estimates that 537 million adults currently live with diabetes, which is projected to increase to 853 million by 2050 [1]. In India, cases have surged from 33 million in 2000 to 72 million in 2021, with projections of 125 million by 2045, posing a significant public health challenge [2]. Addressing this has become a critical priority for India's healthcare system. Given this alarming increase, T2D remission, defined as maintaining glycated hemoglobin (HbA1c) levels <48 mmol/mol (6.5%) for at least three months without glucose-lowering medications, is gaining importance [3].

There is growing interest in non-pharmacological interventions for achieving remission [4,5]. Non-pharmacological strategies, especially lifestyle interventions focusing on diet and weight management, are central to remission efforts [5,6]. A recent position statement by the American College of Lifestyle Medicine stated that remission rates of nearly 50% are achievable through lifestyle changes [7]. Trials have shown that Mediterranean, low-carbohydrate, ketogenic, and plant-based diets effectively lower HbA1c and improve remission rates [8]. Additionally, large-scale trials have emphasized the role of behavioral therapy in achieving T2D remission, supporting a multidisciplinary approach for diabetes management [9]. However, most studies have focused on single interventions, mostly low-calorie diets, with medication withdrawal [4,5]. Despite the success of these approaches in Western populations, there are limited data on their effectiveness in India, where genetic and lifestyle factors place the population at higher risk. Existing interventions may not be directly applicable to the Indian population because of differences in genetics, phenotypes, and cultures. There is a critical need for culturally sensitive and tailored interventions to improve remission rates and health outcomes in India. Furthermore, research identifying predictors of T2D remission in this population remains limited [10].

This study addressed this gap through a retrospective analysis of patients enrolled in an intensive lifestyle intervention program, providing valuable real-world insights into its effectiveness in a large and diverse Indian cohort. The novelty of the intervention lies in its multidisciplinary approach, integrating diet, exercise, psychological support, and medical management, all of which are adapted to the Indian context. This study also aimed to identify predictors of T2D remission to guide culturally appropriate diabetes management strategies.

Materials and methods

Study design and setting

This study was conducted at the Freedom from Diabetes clinic, which operates on a one-year online subscription-based diabetes management model. The complete records of 2384 individuals with T2D enrolled between May 2021 and August 2023 across 263 Indian cities who met the eligibility criteria, were extracted.

Eligibility criteria

Participants aged 30–75 years with a confirmed diagnosis of T2D and on oral hypoglycemic agents (OHAs) were included in the study; those on external insulin therapy were excluded. Drug-naïve patients with HbA1c levels of ≥6.5% were also included. Additional inclusion criteria included a body mass index (BMI) of ≥23 kg/m² and the availability of data from at least three consultations over a one-year program duration. Exclusion criteria comprised individuals with pancreatitis or drug-induced diabetes (such as steroid-induced diabetes), and other types of diabetes (including type 1 diabetes mellitus, diabetes insipidus, maturity-onset diabetes of the young, latent autoimmune diabetes in adults, or gestational diabetes). Patients with advanced complications, such as nephropathy (eGFR <30 mL/min/1.73 m² or urine microalbumin >1000 mg), severe retinopathy (severe non-proliferative or proliferative diabetic retinopathy), significant neuropathy (including complete numbness or sensory loss, amputations, ulcers, foot deformities, or Charcot foot), or peripheral arterial disease, were also excluded. Individuals with a known history of cancer, pregnant or lactating women, those who had been hospitalized for diabetes-related complications in the past six months, and those with incomplete or missing data were also excluded.

The patient selection process is illustrated in Fig 1. Of the 7,458 participants initially enrolled, 3,997 were excluded due to fewer than three follow-up visits, indicating dropout or minimal engagement. An additional 1,077 participants were excluded owing to incomplete or missing data, resulting in a final sample of 2,384 participants.

Measurements

Baseline and one-year follow-up data were obtained from the electronic medical records of the clinic. The data for the present analysis were accessed on September 14, 2024.

Anthropometric and sociodemographic. Data pertaining to sociodemographic variables (including age, sex, marital status, education, and occupation) and anthropometric measurements (specifically weight and height) were obtained
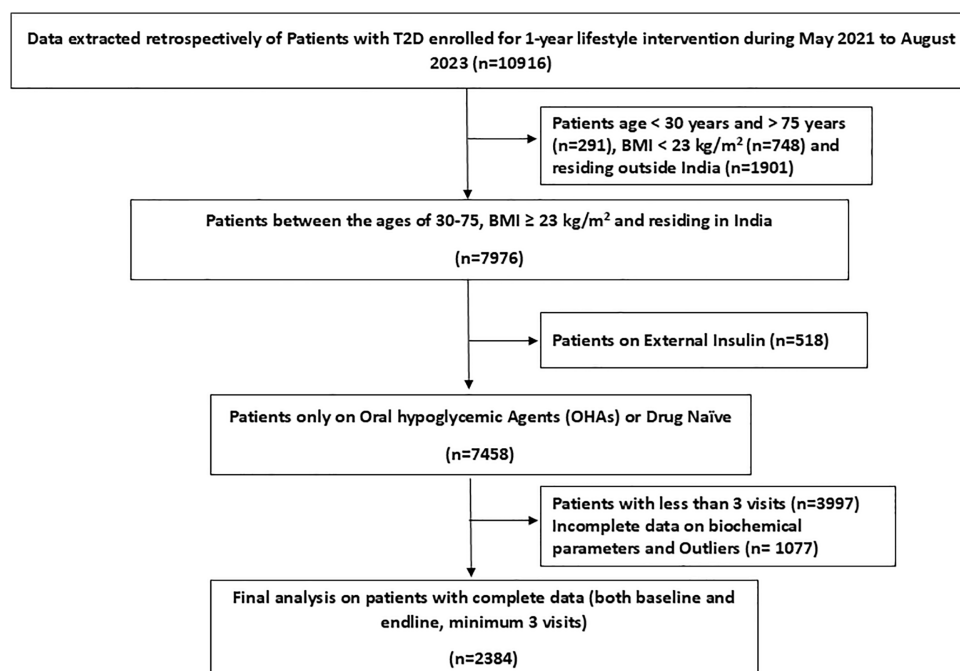

Fig 1. Flowchart depicting the selection procedure of patients for the study.

https://doi.org/10.1371/journal.pone.0333114.g001

through self-reporting. To ensure accuracy, the participants received detailed instructions on the weight and height measurements. Weight was recorded as the average of three measurements, and BMI was calculated.

Biochemical. Data on HbA1c, fasting blood glucose (FBG), and fasting insulin were extracted from biochemical reports uploaded by participants and stored in a centralized data management software. Patients were asked to complete the tests at laboratories accredited by the National Accreditation Board for Testing and Calibration Laboratories (NABL), ensuring alignment with international HbA1c assay standards (e.g., National Glycohemoglobin Standardization Program (NGSP) and International Federation of Clinical Chemistry and Laboratory Medicine (IFCC)). The mobile application used for participant monitoring was integrated with the data management system, enabling real-time tracking and quality control of the submitted reports. Homeostatic Model Assessment of Insulin Resistance (HOMA-IR) and Homeostatic Model Assessment of β-cell function (HOMA-β) were calculated using standard formulae and analyzed in a subset of patients with available fasting insulin data (n = 1897) [11]. Remission was defined as maintaining HbA1c < 6.5% for at least three months without the use of glucose lowering medications in patients on OHAs and those who were drug-naïve [3]. As a program prerequisite, all participants were required to own a glucometer, and digital weighing scale for daily self-reporting of blood glucose level (BGL) and weight.

Intervention

The one-year ILI was structured into four phases, each focusing on four core components: dietary modification, physical activity, psychological support, and medical management. The detailed protocol has been previously described [12].

Each participant was assigned to a six-member care team comprising a physician, dietitian, physical therapist, psychologist, mentor (a past program participant), and monitor (for follow-up and scheduling). At baseline, the core team (physician, dietitian, and physical therapist) set individualized health goals: the physician set HbA1c targets, the dietitian determined weight loss and BMI goals, and the physical therapist prescribed exercise targets considering any pre-existing conditions. These initial goals covered the first six months and were revised midway to establish advanced goals for the remaining six months.

Dietary intervention emphasized a plant-based diet (lentil-based recipes, sprouts, and vegetable salads) tailored to individual BMI and health conditions. Phase 1 emphasized a balanced alkaline diet rich in vegetables, antioxidants, and phytonutrients, with a caloric intake of 1200–1400 kcal/day. In Phase 2, intermittent fasting and juice fasting were introduced for all participants. Juice fasting days limited the intake to 300–500 kcal to support targeted BMI reduction. The primary goals of dietary modification were to detoxify and alkalize the body and gradually reduce calorie intake through intermittent fasting and juice fasting to promote weight loss [13,14]. After achieving their initial BMI goals, participants transitioned to a 1400–1600 kcal/day diet with 1–1.2 grams of protein per kilogram of body weight to support muscle gain alongside exercise. The final phase focused on long-term glycemic control, increasing caloric intake to 1600–1800 kcal/day, with additional protein as per exercise needs, under the supervision of a dietitian and a physical therapist. This stage aimed to help participants sustain weight loss and maintain their dietary and exercise routines.

The diet plan was complemented with exercises to improve strength, flexibility, and stamina. Phase 1 emphasized improving lymphatic circulation, muscle activation, and anti-gravity exercises, including warm-ups, *Sooryanamaskaras* (sun salutations), super brain yoga [15] and palm planks, for post-meal glycemic control. Phase 2 emphasized on muscle gain, weight loss, and core strengthening. Phase 3 introduced personalized activities, such as swimming, running, cycling, or yoga, based on comorbidities, age, and preferences for athletic specializations. In the final phase, periodized plans were implemented to sustain strength, stamina, and flexibility.

Psychological support was aimed at stress and anxiety management and enabled mind-body awareness. This intervention comprised of online group therapy sessions and individual counseling sessions by trained psychologists (upon request by patients) using specific therapeutic approaches, including cognitive behavior therapy (CBT), rational emotional behavior therapy (REBT), neuro-linguistic programming (NLP), clinical hypnotherapy, life coaching, and *pranic* healing [16].

Finally, medical management included physician-directed daily medication adjustments via a dedicated mobile application based on self-reported glucose readings, correction of micronutrient deficiencies through supplementation, quarterly physician consultations, and ongoing care for pre-existing comorbidities. Medication tapering was performed in a stepwise manner, tailored to each participant's clinical progress, and supported by daily BGL submitted via a mobile application. Treating physicians closely monitored BGL trends to make timely dose modifications. The deprescription process was informed by the RSSDI–ESI Therapeutic Wheel, prioritizing the withdrawal of sulfonylureas and insulin while continuing metformin or DPP-4 inhibitors when clinically appropriate [17].

Mode of delivery. A dedicated smartphone application enabled patients to interact with their expert team through voice calls, video calls, and text messages. Clinical data, including self-monitored blood glucose entries from the mobile application and electronic medical records, were linked using a unique participant ID generated at enrollment. The mobile app was integrated with a central data system to enable secure real-time synchronization. At the time of enrollment in the intervention program, participants digitally consented to the use of their anonymized data for research and quality improvement purposes as part of routine onboarding.

During the intervention period, patients were required to regularly report vital signs (blood glucose and weight) through the application, allowing clinicians to adjust medications as needed and guide the diet and exercise intervention. The application also provided region-specific plant-based recipes and pre-recorded exercise and meditation audios, supporting personalized diet, exercise, and stress management plans.

Adherence was supported through a structured care model that combined daily self-monitoring of BGL with continuous engagement from the care team. Participants received weekly or fortnightly consultations with dietitians and physical activity coaches, which later transitioned to monthly and quarterly physician reviews. A mobile application enabled real-time tracking and communication. On average, participants received 63 calls annually and attended monthly online group sessions focused on education and motivation, helping sustain adherence throughout the intervention.

Ethical approval for this study was obtained from the Institutional Ethics Committee (FFDRF/IEC/2024/7), which also waived the requirement for additional written informed consent in accordance with the national guidelines for retrospective research involving minimal risk. This study is registered with the Clinical Trials Registry of India (CTRI/2024/03/064596). The authors had no access to personally identifiable information, thereby ensuring participant confidentiality. This study was conducted in accordance with the Declaration of Helsinki and its amendments.

Statistical analyses

Categorical variables are presented as frequencies and percentages and continuous variables as medians with interquartile ranges owing to the skewed data distribution. The % change was calculated as the final value minus the initial value divided by the initial value multiplied by 100 to adjust for baseline differences. Pre- and post-intervention comparisons, both for the total cohort and subgroup analyses, were conducted using a linear mixed-effects model (LMM) to account for repeated measurements and adjust for relevant covariates. To account for multiple comparisons across outcome variables, we applied the Benjamini–Hochberg (BH) procedure to control the false discovery rate at 5%. BH-adjusted p-values were computed separately for each set of comparisons (Time, Group, and Group×Time effects) in the LMMs. Adjusted p-values <0.05 were considered statistically significant [18].

The chi-square test was used to examine the associations between categorical variables. Variables showing significant bivariate associations with remission were included in the multivariable logistic regression analysis to identify independent predictors of diabetes remission (yes/no): age, HbA1c, medication status, weight change, HOMA-IR, juice fasting, intermittent fasting status, and disease duration. Continuous variables were categorized using clinically relevant thresholds (e.g., HbA1c <7% [19], weight loss >10% [20], and HOMA-IR ≥2.5 [21]) to enhance interpretability. For diabetes duration, a 6-year cut-off was applied based on existing evidence suggesting higher remission rates in patients with shorter disease duration [22]. This threshold enabled meaningful subgroup comparisons, despite the

cohort's median duration of 7.6 years. Statistical analyses were performed using the IBM SPSS ver. 21, with statistical significance set at $p < 0.05$.

Patient and public involvement

Patients and/or the public were not involved in the design, conduct, reporting, or dissemination of this research.

Results and discussion

Baseline characteristics of the study population

Sociodemographic and anthropometric parameters along with the medication status of the population (n = 2384) at the start of the intervention (baseline) are shown in Table 1. The median age of the patients was 51 years (interquartile range [IQR]: 44.0, 58.0) years with 60.1% males. The median diabetes duration was 7.6 (IQR: 3.6, 12.3) years. Median BMI, HbA1c levels, FBG, fasting insulin, HOMA-IR, and HOMA-β were 27.0 (IQR: 24.9, 29.9) kg/m^2, 7.5 (IQR: 6.7, 8.7) %, 130.6 (IQR: 111.0, 157.0) mg/dl, 9.5 (IQR: 6.4, 14.4) μU/ml, 3.2 (IQR: 2.0, 5.1), and 51.1 (IQR: 29.3, 87.6), respectively. Poor glycemic control (HbA1c ≥ 7%) was observed in the majority of the population (67.3%), despite 88.1% being on OHAs. The median HbA1c levels in drug-naïve and OHA-treated patients were 6.9 (IQR: 6.5, 7.5) % and 7.6 (IQR: 6.8, 8.9) %, respectively.

Post-intervention improvements in anthropometric and biochemical parameters based on remission status

Post-intervention, 31.2% (n = 744) of the participants achieved diabetes remission. Among drug-naïve participants, HbA1c improved significantly after the intervention [post-intervention: 6.0% (IQR: 5.6–6.3) vs. baseline: 6.9% (IQR: 6.5–7.5); $p < 0.05$], highlighting the effectiveness of lifestyle modification alone in improving glycemic control.

Table 2 provides a detailed comparison of anthropometric and biochemical parameters between the remission and non-remission groups at both the baseline and post-intervention, along with estimates from the LMM analysis. From baseline to post-intervention, the intervention resulted in significant improvements in weight, BMI, HbA1c, FBG, fasting insulin, and HOMA-IR across the entire cohort; no significant change was observed for HOMA-β.

Groupwise, significant differences were observed between the remission and non-remission group, where at both time points, participants in the remission group consistently had lower weight, BMI, HbA1c, FBG, fasting insulin, HOMA-IR, and higher HOMA-β values (all $p < 0.05$), indicating better glycemic and metabolic status.

Interaction analysis (Group x time) showed that participants in the remission group experienced a significantly greater reduction in weight, BMI, HbA1c, fasting insulin, and HOMA-IR (all $p < 0.05$). The changes in FBG and HOMA-β did not differ significantly between the groups ($p > 0.1$). However, the relatively lower FBG levels and higher HOMA-β in the remission group suggested better glycemic control and preservation of β-cell function compared to the non-remission group.

Among the adjusted covariates, younger age was significantly associated with higher weight, BMI, FBG, and HOMA-IR (all $p < 0.05$). Regardless of time and remission status, females had lower weight and higher BMI than males ($p < 0.05$), likely due to the height difference in the two sexes. Additionally, longer diabetes duration was associated with higher HbA1c and FBG levels and lower fasting insulin, HOMA-IR, and HOMA-β ($p < 0.05$).

Sustainability of glycemic control and remission Post-OHAs discontinuation

At one-year follow-up, 41.4% of participants had discontinued all OHAs and remained off-medication for a median duration of 9 months (IQR: 5.0–11.3). Overall, 744 participants (31.2%) achieved diabetes remission, defined as maintaining HbA1c < 6.5% without OHAs for at least three months.

Among drug-naïve participants (n = 283; 11.9% of the cohort), the overall remission rate was 83%. Of the total, 22.9% (n = 65) had baseline HbA1c < 6.5%, and 21.9% (n = 62) maintained this level post-intervention. Excluding these individuals, the true remission rate, defined as a reduction from HbA1c ≥ 6.5% (n = 218) to < 6.5% without medications, was 79.3%

Table 1. Baseline characteristics of the study population.

Parameter		N (%)
Anthropometric, Socio-demographic, and Clinical Characteristics; n = 2384		
Age (years)	≤50	1175 (49.3)
	>50	1209 (50.7)
Sex	Male	1432 (60.1)
	Female	952 (39.9)
Marital status	Married	2188 (91.8)
	Unmarried	67 (2.8)
	Widowed/Divorced	129 (5.4)
Education	Up to 12 years of schooling	105 (4.4)
	Graduate	1005 (42.2)
	Post-graduate and above	1191 (50.0)
	Others*	83 (3.5)
Occupation	Employed	1633 (68.5)
	Homemaker	425(17.8)
	Retired	227 (9.5)
	Others*	99 (4.2)
Family history of diabetes	Yes	1877 (78.7)
	No	507 (21.3)
BMI classification	Overweight (BMI 23.0–24.9 kg/m²)	604 (25.3)
	Obese (BMI ≥ 25.0 kg/m²)	1780 (74.7)
Glycemic Parameters and Medication Status n = 2384		
HbA1c (%)	<7.0	779 (32.7)
	≥7.0	1605 (67.3)
Fasting Blood Glucose (mg/dl)	<100	288 (12.1)
	≥100	2096 (87.9)
Fasting Insulin (µU/ml); n = 1897 [23]	<25	1795 (94.6)
	≥25	102 (5.4)
HOMA-IR; n = 1897 [21]	<2.5	669 (35.3)
	≥2.5	1228 (64.7)
Medication status	OHAs	2101 (88.1)
	Drug naive	283 (11.9)

Data are presented as frequency and %; BMI, body mass index; OHAs, oral hypoglycemic agents; HbA1c, glycated hemoglobin; HOMA-IR, homeostatic model assessment of insulin resistance; [21,23] references for corresponding cutoff values of the parameters. Fasting Insulin and HOMA-IR data were reported for a subset (n = 1897) for which complete data (pre- and post-intervention) for fasting insulin were available. *Did not share the details.

https://doi.org/10.1371/journal.pone.0333114.t001

(n = 173). These individuals sustained HbA1c < 6.5% for a median duration of 8.6 months (IQR: 7.6–9.5), while 20.6% (n = 45) remained above the threshold of 6.5%. In comparison, participants on OHAs had a significantly lower remission rate of 24.2%.

Remission and its association with parameters

To further explore factors associated with remission, bivariate analysis was performed (Fig 2a, 2b). Remission was more likely in participants aged ≤50 years, with BMI ≥ 25 kg/m², baseline HbA1c < 7%, disease duration ≤6 years, and drug-naïve

Table 2. Comparison of clinical and biochemical parameters at baseline and post-intervention based on remission status.

Outcome	Group	Baseline	Post-intervention	% Change (95% CI)	Model Effect	Estimate (95% CI)	BH adjusted p value¥
Weight (kg)	Total cohort	75.0 (68.0, 84.0)	70.3 (63.4, 78.5)	−6.0 (−6.3, −5.8)	Time (Baseline vs post-intervention)	4.12 (3.90, 4.35)	<0.001
	Remission	76.0 (69.0, 85.0)	70.0 (63.0, 77.2)	−8.5 (−9.1, −8.1)	Group (Remission vs non-remission)	−1.55 (−2.59, −0.51)	0.005
	Non-Remission	74.3 (67.7, 84.0)	70.5 (64.0, 79.0)	−5.2 (−5.6, −4.9)	Group * Time	2.77 (2.37, 3.17)	<0.001
					Age	−0.15 (−0.20, −0.10)	<0.001
					Sex (Female/Male)	−7.20 (−8.19, −6.22)	<0.001
BMI (kg/m²)	Total cohort	27.0 (24.9, 29.9)	25.2 (23.5, 27.9)	−6.0 (−6.3, −5.9)	Time (Baseline vs post-intervention)	1.53 (1.44, 1.61)	<0.001
	Remission	27.4 (25.3, 30.7)	24.9 (23.3, 27.7)	−8.6 (−9.3, −8.3)	Group (Remission vs non-remission)	−0.36 (−0.70, 0.03)	0.031
	Non-Remission	26.8 (24.0, 29.0)	25.3 (23.5, 28.0)	−5.2 (−5.6, −5.0)	Group * Time	1.01 (0.86, 1.17)	<0.001
					Age	−0.04 (−0.06, −0.02)	<0.001
					Sex (Female/Male)	1.69 (1.37, 2.00)	<0.001
HbA1c (%)	Total cohort	7.5 (6.7, 8.7)	6.4 (5.9, 7.0)	−13.5 (−14.1, −12.8)	Time (Baseline vs post-intervention)	1.30 (1.21, 1.38)	<0.001
	Remission	6.9 (6.4, 7.8)	5.9 (5.6, 6.1)	−15.3 (−16.4, −14.3)	Group (Remission vs non-remission)	−1.00 (−1.07, −0.93)	<0.001
	Non-Remission	7.9 (7.0, 9.1)	6.8 (6.3, 7.3)	−12.4 (−13.3, −11.6)	Group * Time	0.19 (0.05, 0.34)	0.008
					Age	−0.007 (−0.110, −0.004)	<0.001
					Diabetes duration	0.02 (0.015, 0.026)	<0.001
FBG (mg/dl)	Total cohort	130.6 (111.0,157.0)	116.3 (101.7,134.0)	−10.3 (−11.6, −9.3)	Time (Baseline vs post-intervention)	19.76 (17.58, 21.93)	<0.001
	Remission	119.0 (104.7,136.9)	103.0 (94.0, 114.6)	−13.2 (−14.5, −11.2)	Group (Remission vs non-remission)	−22.46 (−24.91, −20.01)	<0.001
	Non-Remission	138.0 (116.0, 165.9)	124.1 (108.6, 143.0)	−8.8 (−10.3, −7.4)	Group * Time	0.87 (−3.06, 4.79)	0.777
					Age	−0.40 (−0.51, −0.28)	<0.001
					Diabetes duration	0.58 (0.39, 0.77)	<0.001
Fasting Insulin (µU/ml)[a]	Total cohort	9.5 (6.4,14.4)	7.9 (5.1,11.6)	−15.9 (−18.3, −13.2)	Time (Baseline vs post-intervention)	1.81 (1.42, 2.20)	<0.001
	Remission	10.5 (7.1, 15.6)	7.3 (5.0, 11.7)	−26.6 (−30.5, −23.1)	Group (Remission vs non-remission)	−0.94 (−1.64, −0.24)	0.009
	Non-Remission	9.2 (6.1,14.0)	8.0 (5.1, 11.6)	−11.4 (−14.3, −8.9)	Group * Time	1.48 (0.77, 2.20)	<0.001
					Age	−0.02 (−0.050, 0.008)	0.153
					Diabetes duration	−0.16 (−0.21, −0.11)	<0.001
HOMA-IR[a]	Total cohort	3.2 (2.0, 5.1)	2.3 (1.4,3.5)	−24.3 (−27.7, −21.5)	Time (Baseline vs post-intervention)	1.09 (0.93, 1.25)	<0.001
	Remission	3.1 (2.0, 5.0)	1.9 (1.2, 3.0)	−37.3 (−41.2, −32.8)	Group (Remission vs non-remission)	−0.84 (−1.09, −0.59)	<0.001
	Non-Remission	3.2 (2.0, 5.2)	2.4 (1.5, 3.7)	−19.7 (−22.8, −16.3)	Group * Time	0.40 (0.09, 0.70)	0.013
					Age	−0.02 (−0.03, −0.01)	0.002
					Diabetes duration	−0.04 (−0.05, −0.02)	<0.001

(Continued)

Outcome	Group	Baseline	Post-intervention	% Change (95% CI)	Model Effect	Estimate (95% CI)	BH adjusted p value¥
HOMA-β[a]	Total cohort	51.1 (29.3,87.6)	52.8 (32.4,85.2)	3.3 (0.05, 7.30)	Time (Baseline vs post-intervention)	−12.37 (−36.61, 11.86)	0.317
	Remission	71.0 (42.9, 113.2)	71.3 (44.9, 112.1)	2.9 (−1.2, 11.4)	Group (Remission vs non-remission)	23.89 (16.50, 31.29)	<0.001
	Non-Remission	44.9 (26.5, 75.1)	47.3 (29.5, 75.8)	3.4 (−1.0, 8.0)	Group * Time	8.57 (−36.98, 54.12)	0.710
					Age	0.30 (−0.05, 0.66)	0.103
					Diabetes duration	−1.37 (−1.96, −0.79)	<0.001

status (Fig 2a). Other post-intervention factors associated with remission were adherence to juice and intermittent fasting, HbA1c improvement of >15%, weight loss of >10%, and reduction in insulin resistance (HOMA-IR <2.5) (p<0.05) (Fig 2b). No sex-wise association was observed with remission (p>0.1).

Post-intervention, the improvement in HbA1c (>15% decrease) was similar between drug-naïve patients (45.9%) and those on OHAs (45.4%) (p>0.1), indicating the efficacy of the intervention irrespective of the initial medication status. However, post-intervention weight loss (>10%) was significantly higher in drug-naïve patients (31.8%) than in those receiving OHAs (24.2%); (p = 0.005).

Although remission was significantly associated with weight loss, 58 patients (22.8%) who gained weight post-intervention (n = 254) also achieved remission. The median weight gain in these patients was 1.5 (IQR; 1.0, 3.0) kg. The median diabetes duration and HbA1c level at baseline were 3.7 (IQR: 2.9, 7.2) years and 6.6 (IQR: 6.0, 7.3) %, respectively. Thirty-one percent of these participants were drug naïve.

We further explored the relationship between remission status, decreased HbA1c level, and weight loss (S1A, S1B, S1C Fig). Greater weight loss and decreased HbA1c levels were associated with an increased remission rate (S1A, S1B Fig). A significant positive association between weight loss and HbA1c levels (p <0.05) was also observed (S1C Fig).

Predictors of remission

Binomial logistic regression was performed to assess predictors of remission. The analysis was done on a subset of patients (n = 1897) with the complete data (pre-post-intervention) for fasting insulin, used to calculate HOMA-IR. A shorter disease duration, younger age, drug-naïve status, good HbA1c control at baseline, juice fasting, >10% weight loss, and lower insulin resistance (HOMA-IR) post-intervention were significant predictors of remission (p<0.05) (Fig 3).

Discussion

The increasing prevalence of T2D and its associated comorbidities requires effective alternatives to conventional pharmacotherapy. Multidisciplinary lifestyle interventions have shown promise for T2D management and remission. This study reports the characteristics and population-specific predictors of remission in a large Indian cohort. Unlike previous intervention studies, continued medical management was part of the program, and no drastic dietary changes were introduced
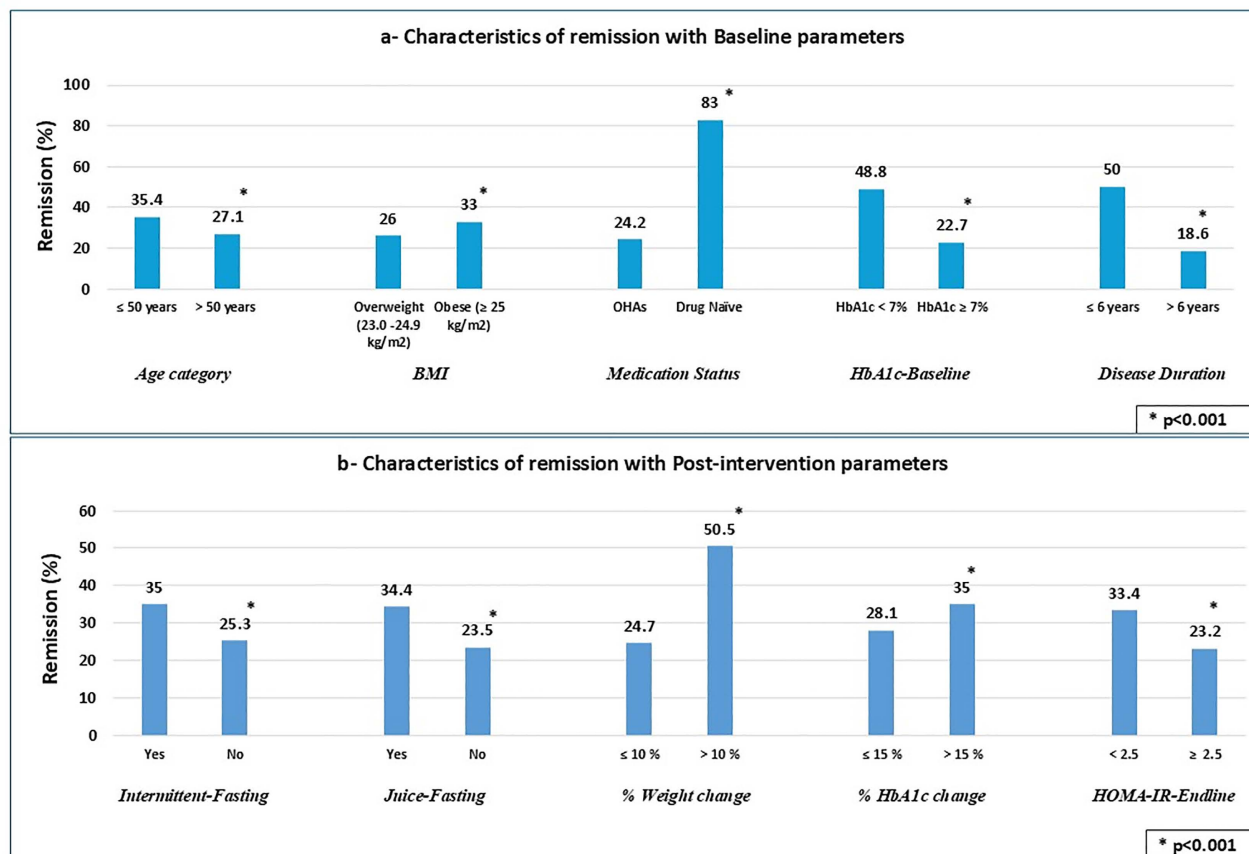
Fig 2. Characteristics of remission. [a] Baseline and [b] post-intervention parameters. OHAs, oral hypoglycemic agents; HbA1c, glycated hemoglobin; HOMA-IR, homeostatic model assessment of insulin resistance; For HOMA-IR, analysis was done on a subset of patients n = 1897 with the complete data (pre-post-intervention) for fasting insulin, used to calculate HOMA-IR.

https://doi.org/10.1371/journal.pone.0333114.g002

to achieve remission. Considering the phenotypic and genotypic diversity of the Indian population compared with Western cohorts, these findings provide valuable evidence supporting non-pharmacological diabetes interventions [4,5,9].

We observed a remission rate of 31.2%, highlighting the potential of lifestyle interventions to achieve diabetes remission. This remission rate aligns with a recent study reporting a 20% remission rate through one-to-one consultations emphasizing weight loss and low-carbohydrate diets [24]. In contrast, higher remission rates have been reported in other randomized controlled trials with smaller cohorts [25,26]. Nevertheless, these findings emphasize the significance of a multidisciplinary approach to T2D remission.

Initial medication status played a significant role, with individuals who had never started medication demonstrating a higher likelihood of remission, thus highlighting the importance of early lifestyle intervention before opting for pharmacotherapy. Additionally, weight loss emerged as the strongest predictor of remission, reinforcing its role in T2D management. This is consistent with other studies that have highlighted diet and weight loss as central strategies for diabetes remission [4,9]. Our study indicated that individuals with a weight loss >10% had a significantly higher remission rate.

Another interesting finding was that some patients achieved remission despite post-intervention weight gain, although this percentage was low. This contrasts with the Personal Fat Threshold theory proposed by Taylor et al., where remission
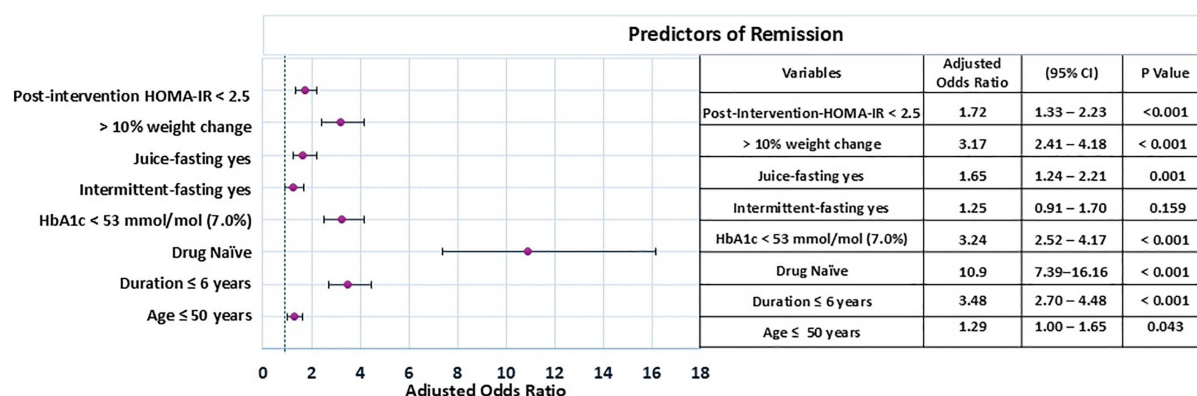
Fig 3. Predictors of T2D Remission (n = 1897). *Footnote:* The forest plot displays adjusted odds ratios (AORs) with 95% confidence intervals (CI) for various parameters to identify predictors. Each circle represents the point estimate, and the horizontal lines show the 95% confidence intervals, which reflect the range within which the true AOR falls. The dashed vertical line at AOR = 1 represents the line of no effect for predictors post-intervention.

https://doi.org/10.1371/journal.pone.0333114.g003

is linked to weight loss in individuals with low BMI [27]. However, the weight gain was minimal and these patients had a mean baseline HbA1c of 6.6%, shorter diabetes duration, and >30% were drug-naïve, possibly contributing to remission. This may also be due to initial weight loss during the intervention. Whether this weight gain is due to muscle building or fat accumulation requires further investigation. Furthermore, a long-term follow-up is required to determine whether remission was sustained in these patients.

Baseline factors such as age (≤50 years), diabetes duration (≤6 years), and baseline HbA1c level (<7.0%) predicted remission, regardless of the initial BMI, highlighting the importance of early intervention. Furthermore, post-intervention improvements in HbA1c and insulin resistance (HOMA-IR) were associated with remission. Our findings, except for younger age (≤50 years), align with the Diabetes Remission Clinical Trial (DiRECT), especially regarding medication use, baseline HbA1c, and weight loss [4,28]. A significant association between reduced HOMA-IR following weight loss and remission was observed, consistent with studies linking low insulin resistance with sustained remission in overweight and obese patients undergoing calorie restriction [29–31]. This emphasizes the need for effective weight management and dietary interventions that specifically address insulin resistance. Intermittent fasting and juice fasting were associated with remission, with juice fasting emerging as a novel predictor. Intermittent fasting has gained attention for its potential impact on metabolic health, and its positive association with remission is consistent with previous research [31]. This finding suggests that incorporating fasting periods into diabetes management may improve T2D outcomes. While some plant-based juices may have potential benefits in cardiovascular diseases because of their nutrient and detoxifying properties, studies suggest that juice fasting may not provide substantial benefits for T2D management, which contradicts our findings [32,33]. Further research is needed to determine the role of juice fasting in glycemic control and overall diabetes management.

In our study, no significant changes in HOMA-β values were observed post-intervention. However, when the baseline HOMA-β values were compared between the remission and non-remission groups, a significant difference was observed in the remission group, with a higher baseline HOMA-β. A higher HOMA-β value at baseline suggests a greater capacity of β-cells to produce insulin, which may have been a key factor in achieving remission in these individuals. Similar observations have been reported in previous studies, in which participants who achieved diabetes remission had higher baseline β-cell function [34,35]. There was no association between sex and remission, indicating that both males and females had an equal chance of achieving remission.

Our study, despite its valuable findings, has several limitations. The retrospective nature of the research and the lack of a control group limit our ability to attribute observed outcomes solely to the intervention. Additionally, the one-year program was a subscription-based service, which may have restricted access to those who could afford it, skewing the participant pool towards individuals with higher socioeconomic status. This group is typically associated with better health outcomes regardless of intervention, which may have impacted the generalizability of the results. Moreover, participants' higher socioeconomic and educational backgrounds might have influenced their ability to adhere to the program, possibly affecting remission rates. We also acknowledge that the exclusion of participants with limited follow-up and missing data may have introduced selection bias. While objective adherence measures were not recorded, adherence was supported by regular consultations, daily glucose tracking, and interactive digital engagement. Although we had a large sample size, the retrospective design may have introduced selection bias and confounding factors, potentially limiting the broader applicability of our findings to the Indian population. Further, the medication tapering followed a structured principle-based clinical protocol (RSSDI–ESI Therapeutic Wheel) and was guided by real-time glycemic trends, yet the retrospective nature of the study may have allowed for some variability in its implementation. Differences in physician judgment, documentation practices, and individual patient responses may have influenced the consistency of OHA withdrawal among participants. While this approach reflects real-world clinical practice, prospective studies with uniform deprescription algorithms and predefined remission criteria are warranted to validate these findings.

On the positive side, the online nature of the program allowed us to reach patients from 263 cities across India, broadening the scope and diversity of our sample. However, this also meant that participants were likely to possess a certain level of digital literacy, which could affect adherence and, consequently, the effectiveness of the intervention. Despite these limitations, our research offers meaningful insights into the real-world effectiveness of intensive lifestyle intervention strategies. Future prospective studies will be crucial in further corroborating these findings.

Conclusions

Our findings add to the growing body of evidence supporting lifestyle interventions as effective strategies for achieving T2D remission in the Indian population. Absolute changes in weight, juice fasting, and post-intervention HOMA-IR were identified as novel remission predictors specific to the Indian population. These results emphasize the importance of personalized interventions targeting multiple aspects of T2D management to improve remission rates and long-term health outcomes. Long-term follow-up and planned randomized controlled trials may help understand the sustainability and feasibility of remission achieved through ILI.

Supporting information

S1 Fig. Associations between remission, HbA1c reduction, and weight loss.
(PDF)

S2 File. Dataset.
(XLSX)

Author contributions

Conceptualization: Pramod Tripathi, Nidhi Kadam.

Data curation: Nidhi Kadam, Thejas Kathrikolly, Baby Sharma.

Formal analysis: Nidhi Kadam, Diptika Tiwari, Anagha Vyawahare.

Investigation: Thejas Kathrikolly.

Methodology: Nidhi Kadam, Thejas Kathrikolly, Diptika Tiwari, Anagha Vyawahare, Baby Sharma.

Project administration: Nidhi Kadam.

Supervision: Pramod Tripathi, Malhar Ganla, Banshi Saboo.

Validation: Pramod Tripathi.

Writing – original draft: Nidhi Kadam, Thejas Kathrikolly.

Writing – review & editing: Pramod Tripathi, Nidhi Kadam, Thejas Kathrikolly, Diptika Tiwari, Anagha Vyawahare, Baby Sharma, Malhar Ganla, Banshi Saboo.

References

1. IDF diabetes atlas, 11th edn. Global diabetes data and statistics. 2025. https://diabetesatlas.org/

2. International Diabetes Federation. IDF diabetes atlas. Brussels, Belgium: International Diabetes Federation; 2021. https://www.diabetesatlas.org/

3. Riddle MC, Cefalu WT, Evans PH, Gerstein HC, Nauck MA, Oh WK, et al. Consensus report: definition and interpretation of remission in type 2 diabetes. Diabetes Care. 2021;44: 2438–44. https://doi.org/10.2337/dci21-0034

4. Lean ME, Leslie WS, Barnes AC, Brosnahan N, Thom G, McCombie L, et al. Primary care-led weight management for remission of type 2 diabetes (DiRECT): an open-label, cluster-randomised trial. The Lancet. 2018;391(10120):541–51. https://doi.org/10.1016/s0140-6736(17)33102-1

5. Taheri S, Zaghloul H, Chagoury O, Elhadad S, Ahmed SH, El Khatib N, et al. Effect of intensive lifestyle intervention on bodyweight and glycaemia in early type 2 diabetes (DIADEM-I): an open-label, parallel-group, randomised controlled trial. Lancet Diabetes Endocrinol. 2020;8(6):477–89. https://doi.org/10.1016/s2213-8587(20)30117-0

6. Tripathi P, Kathrikolly TR. Lifestyle intervention for diabetes remission: a paradigm shift indiabetes care and management. Curr Diabetes Rev. 2024;20(9):e291123224009. https://doi.org/10.2174/0115733998272795231109034141 PMID: 38093443

7. Kelly J, Karlsen M, Steinke G. Type 2 diabetes remission and lifestyle medicine: a position statement from the American college of lifestyle medicine. Am J Lifestyle Med. 2020;14(4):406–19. https://doi.org/10.1177/1559827620930962 PMID: 33281521

8. Esposito K, Maiorino MI, Petrizzo M, Bellastella G, Giugliano D. The effects of a Mediterranean diet on the need for diabetes drugs and remission of newly diagnosed type 2 diabetes: follow-up of a randomized trial. Diabetes Care. 2014;37(7):1824–30. https://doi.org/10.2337/dc13-2899 PMID: 24722497

9. Gregg EW, Chen H, Wagenknecht LE, Clark JM, Delahanty LM, Bantle J, et al. Association of an intensive lifestyle intervention with remission of type 2 diabetes. JAMA. 2012;308(23):2489–96. https://doi.org/10.1001/jama.2012.67929 PMID: 23288372

10. Vijayakumar V, Mavathur R, Sharma MNK. Ethnic disparity and increased prevalence of type 2 diabetes among South Asians: aetiology and future implications for diabetes prevention and management. Curr Diabetes Rev. 2018;14(6):518–22. https://doi.org/10.2174/1573399813666170915132935 PMID: 28914196

11. Wallace TM, Levy JC, Matthews DR. Use and abuse of HOMA modeling. Diabetes Care. 2004;27(6):1487–95. https://doi.org/10.2337/diacare.27.6.1487 PMID: 15161807

12. Tripathi P, Kadam N, Tiwari D, Kathrikolly T, Vyawahare A, Sharma B, et al. The diabetes remission in India (DiRemI) study: protocol for a prospective matched-control trial. PLoS One. 2024;19(6):e0306394. https://doi.org/10.1371/journal.pone.0306394 PMID: 38941311

13. Obert J, Pearlman M, Obert L, Chapin S. Popular weight loss strategies: a review of four weight loss techniques. Curr Gastroenterol Rep. 2017;19(12):61. https://doi.org/10.1007/s11894-017-0603-8 PMID: 29124370

14. Storz MA, Ronco AL, Hannibal L. Observational and clinical evidence that plant-based nutrition reduces dietary acid load. J Nutr Sci. 2022;11:e93. https://doi.org/10.1017/jns.2022.93 PMID: 36405093

15. Sui MCK. Superbrain Yoga. Institute for Inner Studies Publishing Foundation, Inc.; 2012.

16. Turner MJ. Rational emotive behavior therapy (REBT), irrational and rational beliefs, and the mental health of athletes. Front Psychol. 2016;7:1423. https://doi.org/10.3389/fpsyg.2016.01423 PMID: 27703441

17. Hasnani D, Chavda V, Agrawal D, Patni B, David A, Gathe S, et al. Validation of RSSDI therapeutic wheel with clinical experience of Indian physicians. Int J Diabetes Dev Ctries. 2021;42(3):451–8. https://doi.org/10.1007/s13410-021-00998-6

18. Benjamini Y, Yekutieli D. The control of the false discovery rate in multiple testing under dependency. Ann Statist. 2001;29(4). https://doi.org/10.1214/aos/1013699998

19. American Diabetes Association Professional Practice Committee. 2. Classification and diagnosis of diabetes: standards of medical care in diabetes-2022. Diabetes Care. 2022;45(Suppl 1):S17–38. https://doi.org/10.2337/dc22-S002 PMID: 34964875

20. Dambha-Miller H, Day AJ, Strelitz J, Irving G, Griffin SJ. Behaviour change, weight loss and remission of Type 2 diabetes: a community-based prospective cohort study. Diabet Med. 2020;37(4):681–8. https://doi.org/10.1111/dme.14122 PMID: 31479535

21. Gutch M, Kumar S, Razi SM, Gupta KK, Gupta A. Assessment of insulin sensitivity/resistance. Indian J Endocrinol Metab. 2015;19(1):160–4. https://doi.org/10.4103/2230-8210.146874 PMID: 25593845

22. Taylor R, Irvine KM, Barnes AC, Kelly TL, Clark LG, Hollingsworth KG, et al. 218-LB: remission of type 2 diabetes after weight loss in "Normal" weight people—the ReTUNE study. Diabetes. 2022;71(Supplement_1). https://doi.org/10.2337/db22-218-lb

23. Saxena P, Prakash A, Nigam A. Efficacy of 2-hour post glucose insulin levels in predicting insulin resistance in polycystic ovarian syndrome with infertility. J Hum Reprod Sci. 2011;4(1):20–2. https://doi.org/10.4103/0974-1208.82355 PMID: 21772735

24. Unwin D, Delon C, Unwin J, Tobin S, Taylor R. What predicts drug-free type 2 diabetes remission? Insights from an 8-year general practice service evaluation of a lower carbohydrate diet with weight loss. BMJNPH. 2023;6(1):46–55. https://doi.org/10.1136/bmjnph-2022-000544

25. Dave R, Davis R, Davies JS. The impact of multiple lifestyle interventions on remission of type 2 diabetes mellitus within a clinical setting. Obesity Medicine. 2019;13:59–64. https://doi.org/10.1016/j.obmed.2019.01.005

26. Ried-Larsen M, Johansen MY, MacDonald CS, Hansen KB, Christensen R, Wedell-Neergaard A-S, et al. Type 2 diabetes remission 1 year after an intensive lifestyle intervention: a secondary analysis of a randomized clinical trial. Diabetes Obes Metab. 2019;21(10):2257–66. https://doi.org/10.1111/dom.13802 PMID: 31168922

27. Taylor R, Barnes AC, Hollingsworth KG, Irvine KM, Solovyova AS, Clark L, et al. Aetiology of Type 2 diabetes in people with a "normal" body mass index: testing the personal fat threshold hypothesis. Clin Sci (Lond). 2023;137(16):1333–46. https://doi.org/10.1042/CS20230586 PMID: 37593846

28. Thom G, Messow C-M, Leslie WS, Barnes AC, Brosnahan N, McCombie L, et al. Predictors of type 2 diabetes remission in the diabetes remission clinical trial (DiRECT). Diabet Med. 2021;38(8):e14395. https://doi.org/10.1111/dme.14395 PMID: 32870520

29. de Hoogh IM, Oosterman JE, Otten W, Krijger A-M, Berbée-Zadelaar S, Pasman WJ, et al. The effect of a lifestyle intervention on type 2 diabetes pathophysiology and remission: the Stevenshof pilot study. Nutrients. 2021;13(7):2193. https://doi.org/10.3390/nu13072193 PMID: 34202194

30. Umphonsathien M, Rattanasian P, Lokattachariya S, Suansawang W, Boonyasuppayakorn K, Khovidhunkit W. Effects of intermittent very-low calorie diet on glycemic control and cardiovascular risk factors in obese patients with type 2 diabetes mellitus: a randomized controlled trial. J Diabetes Investig. 2022;13(1):156–66. https://doi.org/10.1111/jdi.13619 PMID: 34176234

31. Yang X, Zhou J, Shao H, Huang B, Kang X, Wu R, et al. Effect of an intermittent calorie-restricted diet on type 2 diabetes remission: a randomized controlled trial. J Clin Endocrinol Metab. 2023;108(6):1415–24. https://doi.org/10.1210/clinem/dgac661 PMID: 36515429

32. Gilchrist M, Winyard PG, Aizawa K, Anning C, Shore A, Benjamin N. Effect of dietary nitrate on blood pressure, endothelial function, and insulin sensitivity in type 2 diabetes. Free Radic Biol Med. 2013;60:89–97. https://doi.org/10.1016/j.freeradbiomed.2013.01.024 PMID: 23395779

33. Zheng J, Zhou Y, Li S, Zhang P, Zhou T, Xu D-P, et al. Effects and mechanisms of fruit and vegetable juices on cardiovascular diseases. Int J Mol Sci. 2017;18(3):555. https://doi.org/10.3390/ijms18030555 PMID: 28273863

34. Purnell JQ, Dewey EN, Laferrère B, Selzer F, Flum DR, Mitchell JE, et al. Diabetes remission status during seven-year follow-up of the longitudinal assessment of bariatric surgery study. J Clin Endocrinol Metab. 2021;106(3):774–88. https://doi.org/10.1210/clinem/dgaa849 PMID: 33270130

35. Roncero-Ramos I, Gutierrez-Mariscal FM, Gomez-Delgado F, Villasanta-Gonzalez A, Torres-Peña JD, Cruz-Ares SDL, et al. Beta cell functionality and hepatic insulin resistance are major contributors to type 2 diabetes remission and starting pharmacological therapy: from CORDIOPREV randomized controlled trial. Transl Res. 2021;238:12–24. https://doi.org/10.1016/j.trsl.2021.07.001 PMID: 34298148