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Evaluation of twin health Treatment Program

For Metabolic Disorder

Preface

The Evaluation of Twin Health Treatment Program was initiated by IIT Madras Research Park and authored by Prof. Ashok Jhunjhunwala (President, IIT Madras Research Park), Prof. Mohanasankar Sivaprakasam (Vice President, IIT Madras Research Park) and Prof. Gaurav Raina (Professor, IIT Madras). We would like to express our gratitude to the technical experts from Twin Health team. Through this report, IIT Madras Research Park aims to evaluate the effectiveness of Twin Health's Whole-Body Digital Twin™, in creating a predictive model that provides individualized nutrition, sleep, activity, and breathing guidance to patients. Engagement and Adherence to the recommendations through the Twin Application influences the outcomes of the patient's overall health and wellbeing.

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Executive Summary

The purpose of this technology evaluation report is to assess the effectiveness of the Twin Health's treatment methodology, which aims to reverse, improve, and prevent chronic metabolic diseases, particularly Type 2 Diabetes.

Twin Health holds the patent for this precision treatment platform enabled by Whole Body Digital Twin™. The Whole-Body Digital Twin™ is a dynamic representation of an individual's unique metabolism, built from thousands of data points collected on a daily basis. These data are collected through non-invasive wearable sensors, providing a personalized representation of each individual's unique metabolism.

This report provides an overview of results, including an analysis of various health parameters, recovery rates, medication usage, and food transformation.

- The health parameter analysis focused on tranformation of various health parameters from Day 0 to Day 360.
- The recovery analysis examined the rate at which patient's health parameters improve from abnormal values and reach the optimal range.
- Medication analysis aimed to determine how quickly patients were able to reduce or avoid the consumption of medications.
- Food data analysis was performed to establish correlation between food consumption with HbA1C value, Metabolic Score, Engagement score and Adherence score.

Data from 206 Prime patients and 82 Control patients were analysed, where the Prime patients are diagnosed with a metabolic disorder or Type 2 Diabetes (T2D) enrolled in Randomized Controlled Trial (RCT) of Twin Precision Treatment (TPT). Control patients were not part of the Twin program but were diabetic and consulting other health organizations or doctors

- A total of 8 health parameters were assessed, and by the end of day 360, all the health parameters for the Prime patients were found to be within the optimum range. Additionally, Prime patients showed a 34% reduction in Hemoglobin A1C (HbA1C) and 57.4% reduction in ASCVD 10-Year Risk Score.
- The majority of Prime patients achieved Systolic Blood Pressure below 140 mm Hg and Diastolic Blood Pressure below 90 mm Hg on Day 30 itself.
- The medication analysis considered seven medicines including Insulin. From Day 30 onwards, over 90% of Prime patients had stopped taking all medications.
- For most RCT patients the food transformation - from Red / Orange food to Green food- over a treatment period of 1 year was analysed and found to be effective.

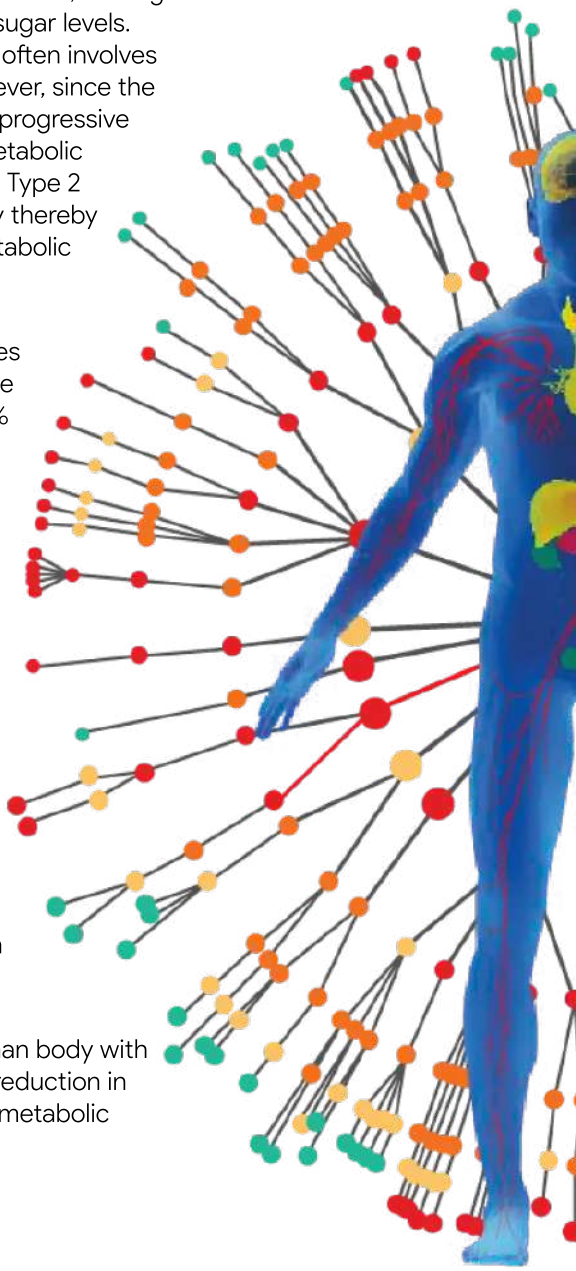
The effectiveness of the Whole-Body Digital Twin™ Technology in improving the disrupted metabolism was evaluated by The American Diabetes Association (ADA) in its release: "Artificial Intelligence Offers Significant Rate of Remission for Type 2 Diabetes Compared to Standard Care" (June 2022).

In conclusion, Twin Health's Whole-Body Digital Twin™ technology has proven to be effective in highly prevalent metabolic conditions such as Type 2 Diabetes, prediabetes, and obesity. It shows significant improvements across high impact conditions like blood pressure by addressing the root cause of damaged metabolism. Medication use was eliminated in nearly all Prime patients. The results provide evidence that daily precision nutrition guidance based on food intake data can benefit patients with Type 2 Diabetes.

Introduction

Metabolic disorders are characterized by abnormalities in the body's ability to release and store energy from food. This prevents the body from using the energy from the digested food, leading to severe damage to body functions, especially the nerves and blood vessels. It can cause various health complications such as obesity, insulin resistance, and Type 2 diabetes.

Metabolic dysfunction is characterized by a reduced response of the body to Insulin, leading to difficulties in the entry of glucose into cells and resulting in elevated blood sugar levels. The conventional approach for its treatment - measures to lower sugar level - often involves managing the symptoms rather than addressing the underlying disease. However, since the root cause is not directly targeted, metabolic syndrome tends to be a lifelong progressive condition, necessitating regular monitoring to ensure proper management. Metabolic disorders increase the risk of developing, heart and blood vessel diseases and Type 2 diabetes. By increasing the metabolic rate to break down food more efficiently thereby facilitating weight loss, metabolic health can be improved thus preventing metabolic disorders



In India, insulin resistance and metabolic syndrome are widely prevalent. Studies have reported that in urban Indian populations, the prevalence in particular age groups were found to be overall 25%. (Approximately 31% in women and 18.5% in men). Another such disorder is Diabetes which shows around 422 million people globally have diabetes, the majority of who live in low-income and middle-income countries. More than 1.6 million deaths were reported directly due to diabetes just in 2020.

A. Factors Contributing to Metabolic Dysfunction

Metabolic dysfunction is influenced by the effects of genetic, environmental, and lifestyle factors. While we can control some of these causes, such as diet and physical activity levels, other causes, such as age and genes, cannot be controlled. Genetic predisposition plays a significant role in metabolic dysfunction. Environmental factors such as pollution, certain chemicals that are found in plastics, pesticides, and personal care products possess endocrine-disrupting properties. Finally, emerging evidence suggests that alterations in the composition and diversity of the gut microbiota, influenced by factors such as diet, antibiotic use, and stress, can impact metabolic health through effects on energy extraction, inflammation, and gut barrier function

The Twin Health program works on treating the metabolic disorder of the human body with proper diet modification, thereby improving metabolic efficiency leading to a reduction in severity of Type 2 diabetes. The program helps in understanding the patient's metabolic conditions guiding towards much healthier food choices and daily activities

B. About Twin Health's Whole-Body Digital Twin™

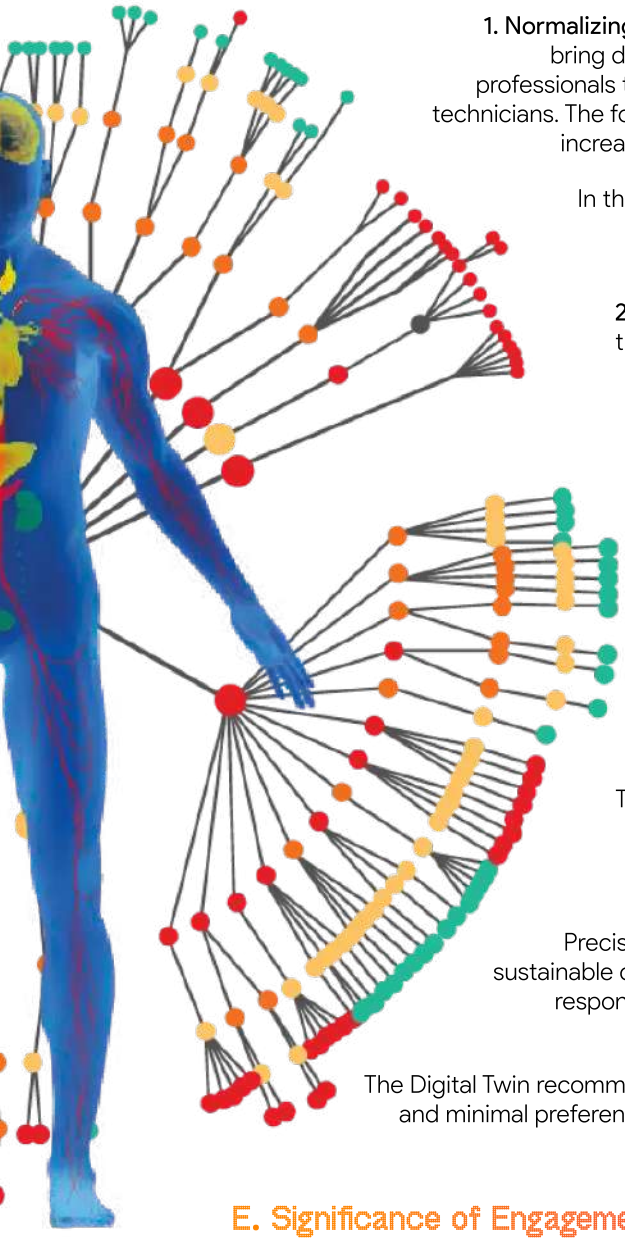
Twin Health uses the Whole-Body Digital Twin™ technology to reverse and prevent multiple chronic diseases using scientific and evidence-based research. The Whole-Body Digital Twin™ is powered by artificial intelligence and is a dynamic representation of an individual's unique metabolism, built from thousands of data points collected daily through non-invasive wearable sensors and self-reported preferences.

The Whole-Body Digital Twin™ is a patient health management platform that accesses the metabolic profile for a patient and bio signals recorded through sensor data and lab test data collected of the patient. The platform receives patient data recorded during the treatment period comprising of food items consumed, medications taken, and symptoms experienced by the patient. It also generates a patient-specific treatment recommendation outlining instructions for the patient to improve their metabolic state that are recommended to the display of the patient in the patient device. Twin Health has patented this precision treatment platform enabled by Whole-Body Digital Twin™ technology **(Publication/Patent Number: EP3996584A1)**.

The Twin Precision treatment program emphasizes in monitoring the diet of every individual to repair and heal the damaged metabolism as unmonitored dieting can be severely harmful.

C. Phases of the Patient's Journey

The 1-year treatment methodology of Twin Health follows a step-by-step procedure to monitor the patient's health, diet, and medications. It adopts a precision treatment with 3 phases organized in such a way, that it normalizes the sugars in 5-6 months, healing the metabolism in the next 6 months, sustaining, or improving organ health in the last phase along with beta cell regeneration towards a diabetes – free life.



1. Normalizing (1 – 6 months): In the initial 3 months of the treatment, the primary target is to bring down the blood glucose, after the assessment of the patient body by health care professionals through body sensors, data from mobile apps and collection of blood sample by technicians. The food characterization will be done to identify and avoid Red foods that can cause increase in the blood glucose levels and subsequently increase the Green food intake.

In the next 3 to 6 months, by studying the patient health responses to the treatment and diet taken as prescribed by Twin Health professional, they reset the goal to reverse the diabetes by healing the damaged metabolism

2. Healing (6 – 12 months): In the forthcoming months, Twin Health professionals tries to reverse the diabetes by improving the function of organ's health there by making the body to secrete the insulin naturally and their body is monitored.

Once the body starts to reverse diabetes, the ways to sustain the reversal is explored for individual patient while the Insulin & medicines are completely stopped and the food transformation slowly occurs from Red to Green.

3. Sustaining (After 12 months): Once the diabetes is reversed, Twin takes the next step to optimize the health by working on diabetic control and permitting the patient to take all the red foods slowly like a nondiabetic patient.

D. Precision Treatment Program

Twin Health offers precision treatment that corrects metabolic damages with the help of FDA approved sensors and AI/ML. It's extensive treatment methodology includes precision nutrition, precision activity, precision sleep, and precision breathing.

Precision Nutrition helps in tracking 87 nutrient elements in each meal and suggests a sustainable diet that optimally combines macro, micro and biota nutrients to predict glucose response to specific foods and provided specific daily food recommendations to avoid glucose spikes.

The Digital Twin recommends activities that are precise to the patient's body based on the health signals and minimal preferences such as precise sleep hours, personalised meditative breathing for a precise duration that can help in overall mental and physical well-being.

E. Significance of Engagement and Adherence in the Evaluation of Twin Health Treatment Technology

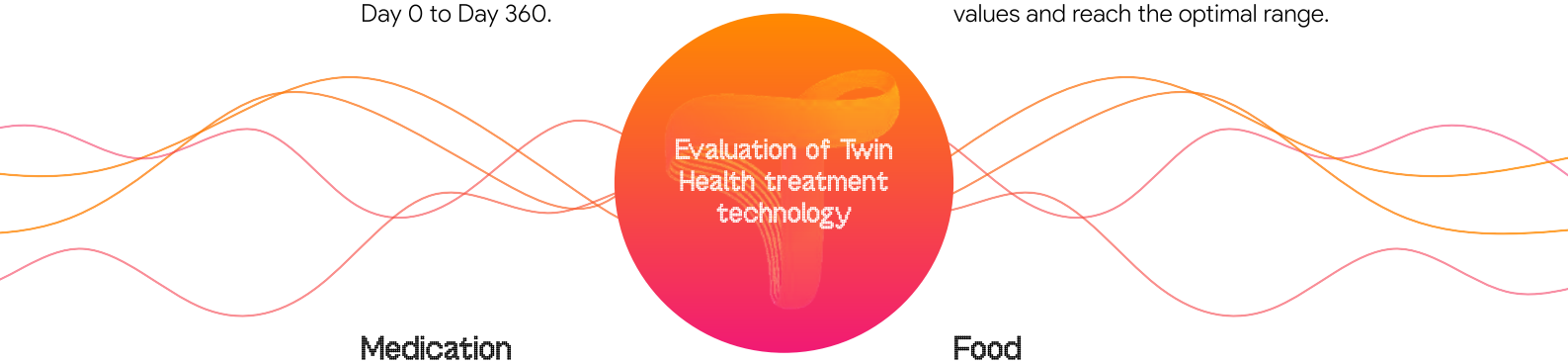
Engagement and Adherence influences the outcomes of Twin Health patients with metabolic disorders. When patients actively participate in their treatment and consistently follow their prescribed regimen, they reduce the risk of complications and enhance their overall health and well-being. The evaluation of the treatment methodology followed by Twin Health's program for reversing metabolic disorders considers various health and recovery analysis, medication, and food consumption of the Twin patients in correlation with the HbA1C value, Metabolic score, Engagement score, Adherence score.

Health parameter analysis

This analysis focused on transformation of various health parameters from Day 0 to Day 360.

Recovery analysis

The recovery analysis examined the rate at which patient's health parameters improve from abnormal values and reach the optimal range.



Medication analysis

Medication analysis aimed to determine how quickly patients were able to discontinue their medications for diabetics.

Food analysis

The food analyses are performed to establish correlation between food consumption with Engagement score, Adherence score, Metabolic Score and HbA1C value.

Twin Precision Treatment (TPT) is a precision nutrition system that utilizes 174 health markers and 3000 daily data points. These are gathered from blood tests and connected devices such as sensor watch, a smart body composition scale and an arm blood pressure meter that measure weight, physical activity, sleep, and sensor glucose values, for achieving remission.

Twin Precision Nutrition (TPN) Program provides participants with a set of specific food recommendations each day to avoid glucose spikes. Patients were also asked to record their food intake on the app each day. Each food item within every meal was logged along with its weight by selecting it from a database of more than 2000 foods.

F. Categorization of Patients

Data for 12 months of 206 Prime patients and 82 Control patients were analysed and inferences were tracked.

Prime patients are with Type 2 Diabetes (T2D) enrolled in Randomized Controlled Trial (RCT) of Twin Precision Treatment (TPT).

Control patients are the ones who are not part of the Twin program but are diabetic and consulting other health organization or doctors.

Results of various analysis

A. Transformation of Health Parameters over 360 Days

Parameters (units)	Optimum range	Patients	Mean								
			Day 0	Day 30	Day 60	Day 90	Day 120	Day 150	Day 180	Day 270	Day 360
HbA1C Hemoglobin A1C (%)	< 6.5% with / without Metformin drug	Control	8.5	8.2	8.3	8.2	8.3	8.2	8.1	8.2	8.2
		Prime	9.0	7.0	6.1	5.6	5.6	5.6	5.7	5.9	5.9
SysBP Systolic Blood Pressure (mm Hg)	< 140mm Hg	Control	134	130	129	132	129	128	130	131	131
		Prime	128	120	118	117	117	117	117	119	119
DiaBP Diastolic Blood Pressure (mm Hg)	< 90mm Hg	Control	87	88	85	87	85	85	85	85	85
		Prime	85	80	79	78	78	78	78	81	80
BMI (Kg/m^2)	< 25 Kg/m^2	Control	28.1	28.7	28.3	28.3	28.0	28.7	28.1	28.1	28.1
		Prime	27.3	26.0	24.9	24.3	28.3	23.6	23.6	23.9	24.5

Table 1 – Comparison for the Change in the Diabetic, Blood Pressure and Weight parameters across the Control patients and Prime patients.

Parameters (units)	Optimum range	Patients	Mean				
			Day 0	Day 90	Day 180	Day 270	Day 360
Triglycerides (mg/dL)	< 150 mg/dL	Control	252	217	225	211	232
		Prime	222	126	128	132	148
LDL Low Density Lipoprotein (mg/dL)	< 130 mg/dL	Control	119	116	118	114	119
		Prime	128	135	130	127	129
HDL High Density Lipoprotein (mg/dL)	> 40 mg/dL	Control	36	35	36	34	38
		Prime	35	38	43	45	44
hs-CRP High sensitivity C-Reactive Protein (mg/L)	< 3 mg/L	Control	4	7	6	5	8
		Prime	2.9	2.9	1.4	1.0	1.3

*Control patients (n = 82) Prime patients (n = 206)

Table 2 – Comparison for the Change in the Lipid and Inflammation parameters across the Control patients and Prime patients.

ASCVD 10-Year Risk Score:

Parameters (units)	Optimum range	Patients	Mean				
			Day 0	Day 90	Day 180	Day 270	Day 360
ASCVD(%) 10-Year Risk Score	< 5%	Control	10.53	10.45	8.83	9.34	9.41
		Prime	8.21	3.76	3.09	3.43	3.49

*Control patients (n = 82) Prime patients (n = 206)

Table 3 – Comparison for the change in the ASCVD 10-Year Risk Score parameter across the Control patients and Prime patients.

Parameters (units)	Optimum range	Patients	Number of Patients				
			Day 0	Day 90	Day 180	Day 270	Day 360
ASCVD(%) 10-Year Risk Score	Low Risk (< 5%)	Control	34	34	38	18	30
		Prime	95	155	164	109	153
	Borderline Risk (5% to < 7.5%)	Control	8	8	8	8	8
		Prime	34	20	24	22	20
	Intermediate Risk (7.5% to < 20%)	Control	26	28	29	15	19
		Prime	58	31	18	12	21
	High Risk (≥20%)	Control	14	12	7	5	11
		Prime	19	0	0	1	2

*Control patients (n = 82) Prime patients (n = 206)

Table 4 – Change in the number of patients ASCVD 10-Year Risk Score value from 0th day to 360th days.

B. Examining Recovery Rate of Health Parameters over Time

Parameters (units)	Optimum range	Patients	No of Patients									
			Day 0	Day 30	Day 60	Day 90	Day 120	Day 150	Day 180	Day 270	Day 360	Not reached
HbA1C Hemoglobin A1C (%)	< 6.5% with / without Metformin drug	Control	10 (12.2%)	3 (3.7%)	3 (3.7%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	2 (2.4%)	61 (74.4%)
		Prime	14 (6.8%)	45 (21.8%)	87 (42.2%)	44 (21.4%)	11 (5.3%)	3 (1.5%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	1 (0.5%)
SysBP Systolic Blood Pressure (mm Hg)	< 140mm Hg	Control	53 (64.6%)	12 (14.6%)	6 (7.3%)	4 (4.9%)	1 (1.2%)	2 (2.4%)	2 (2.4%)	0 (0.0%)	0 (0.0%)	2 (2.4%)
		Prime	178 (86.4%)	25 (12.1%)	2 (1.0%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
DiaBP Diastolic Blood Pressure (mm Hg)	< 90mm Hg	Control	53 (64.6%)	6 (7.3%)	11 (13.4%)	3 (3.7%)	1 (1.2%)	2 (2.4%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	3 (3.7%)
		Prime	156 (75.7%)	41 (19.9%)	5 (2.4%)	4 (1.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Triglycerides (mg/dL)	< 150 mg/dL	Control	25 (30.5%)	0 (0.0%)	7 (8.5%)	0 (0.0%)	0 (0.0%)	5 (6.1%)	3 (3.7%)	4 (4.9%)	0 (0.0%)	38 (46.3%)
		Prime	63 (30.6%)	1 (0.5%)	0 (0.0%)	97 (47.1%)	0 (0.0%)	1 (0.5%)	19 (9.2%)	8 (3.9%)	4 (1.9%)	13 (6.3%)
LDL Low Density Lipoprotein (mg/dL)	< 130 mg/dL	Control	46 (56.1%)	0 (0.0%)	1 (1.2%)	17 (2.07%)	0 (0.0%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	1 (1.2%)	14 (17.1%)
		Prime	110 (53.4%)	0 (0.0%)	0 (0.0%)	30 (14.6%)	1 (0.5%)	1 (0.5%)	10 (4.9%)	8 (3.9%)	7 (3.4%)	39 (18.9%)
HDL High Density Lipoprotein (mg/dL)	> 40 mg/dL	Control	25 (30.5%)	0 (0.0%)	0 (0.0%)	4 (4.9%)	0 (0.0%)	0 (0.0%)	4 (4.9%)	0 (0.0%)	7 (8.5%)	42 (51.2%)
		Prime	36 (17.5%)	0 (0.0%)	0 (0.0%)	47 (22.8%)	0 (0.0%)	1 (0.5%)	53 (25.7%)	21 (10.2%)	6 (2.9%)	42 (20.4%)
hs-CRP High sensitivity C-Reactive Protein (mg/L)	< 3 mg/L	Control	38 (46.3%)	0 (0.0%)	0 (0.0%)	9 (11.0%)	0 (0.0%)	0 (0.0%)	4 (4.9%)	4 (4.9%)	2 (2.4%)	25 (30.5%)
		Prime	151 (73.3%)	1 (0.5%)	1 (0.5%)	20 (9.7%)	1 (0.5%)	1 (0.5%)	17 (8.3%)	8 (3.9%)	3 (1.5%)	3 (1.5%)
BMI (Kg/m²)	< 25 Kg/m²	Control	22 (26.8%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.2%)	2 (2.4%)	1 (1.2%)	0 (0.0%)	56 (68.3%)
		Prime	67 (32.5%)	23 (11.2%)	29 (14.1%)	17 (8.3%)	7 (3.4%)	5 (2.4%)	2 (1.0%)	5 (2.4%)	0 (0.0%)	51 (24.8%)

*Control patients (n = 82) Prime patients (n = 206)

Note: After patients reach the optimum range, they are not considered in the following months.

Table 5 – Comparison for the rate at which predominant health parameter reached the optimum range by the Control patients and Prime patients

C. Assessing Reduction in Patient's Medication Usage

Medication	Patients	No of Patients								
		Day 0	Day 30	Day 60	Day 90	Day 120	Day 150	Day 180	Day 270	Day 360
Insulin	Control	3	3	3	3	3	3	3	9	6
	Prime	11	0	0	0	0	0	0	0	1
Sulfonyl	Control	54	54	54	55	55	55	55	41	39
	Prime	83	0	0	0	0	0	0	0	0
Thiazol	Control	10	10	10	10	10	10	9	6	5
	Prime	15	0	0	0	0	0	0	0	0
Glucosidase	Control	23	23	23	23	23	23	21	18	17
	Prime	15	0	0	0	0	0	0	0	0
SGLT2_Inhibitor	Control	2	2	2	2	2	2	2	1	0
	Prime	11	0	0	0	0	0	0	0	0
DPP-4_Inhibitor	Control	34	34	34	31	31	31	35	31	24
	Prime	68	0	0	1	0	0	0	0	2
Metformin	Control	77	77	77	76	76	76	75	58	57
	Prime	149	21	14	14	14	19	18	12	6
Not Taking Medicine	Control	3	3	3	4	4	4	4	0	10
	Prime	41	185	192	192	192	187	188	194	162

*Control patients (n = 82) Prime patients (n = 206)

Table 6 – Change in the number of patients taking medications for Type 2 diabetes from 0th day to 360th days.

D. Correlation between Food Consumption and Health Metrics

Metric score / Values	Mean														
	Apr '21	May '21	Jun '21	Jul '21	Aug '21	Sep '21	Oct '21	Nov '21	Dec '21	Jan '22	Feb '22	Mar '22	Apr '22	May '22	Jun '22
Food rating value	1.36	1.49	1.75	1.96	1.90	1.83	1.78	1.73	1.65	1.65	1.73	1.84	1.80	1.84	1.99
Engagement score	85%	84%	83%	79%	79%	73%	71%	67%	64%	58%	58%	48%	46%	43%	40%
Adherence score	78%	76%	77%	72%	69%	62%	55%	50%	47%	42%	43%	35%	30%	31%	29%
Metabolic score	82.9	79.9	79.9	82.0	85.9	86.4	86.9	86.5	86.7	85.7	85.2	84.5	83.9	82.9	82.4
HbA1c (%)	6.5	6.8	6.0	5.9	5.7	5.6	5.6	5.7	5.9	6.0	5.9	6.0	6.1	6.1	6.3

Optimum Range - Hemoglobin A1C (HbA1C): <6.5% with or without Metformin drug | Metabolic score: >80

Table 7 – Change in Food rating value, Engagement score, Adherence score, Metabolic score and HbA1c of 100 RCT patients over a 1-year treatment period from April 2021 to June 2022

Note:

Food rating value	0 to 1	> 1 to 2	>2 to 3
Food colors	Red (Must not eat)	Orange (Good to eat)	Green (Must eat)

Analysis of various parameters in accordance with engagement and adherence

A. Transformation of Health Parameters over 360 Days

The Twin treatment analysis gathers the patient's health parameter values during the treatment period with constant monitoring of blood glucose levels, insulin resistance and overall health observation. In addition, the blood samples are collected periodically. Data is also traced from mobile phones where the health signals are received from the whole–body digital twin to which patient feed the data.

Comparison for the changes in the Diabetic, Blood Pressure, Lipid, Inflammation and Weight parameters at 0, 30, 60, 90, 120, 150, 180, 270, 360 days across the Control and Prime patients are analysed.

Represent number of patients data available on specific days

Represent Average Parameter Values

X Axis – Days of treatment, **Y Axis** – Health Parameter Value

Diabetic Parameter

1. **Hemoglobin A1C (HbA1C):**

HbA1C represents the Glycated Hemoglobin. HbA1c depicts the last 2-to-3-month average blood glucose.
Optimum Range with or without Metformin drug is <6.5 %

Fig 1- Change in Hemoglobin A1C (HbA1C) from 0th day to 360th days of Control and Prime patients

The mean HbA1C of the 206 Prime patients decreased from 9.0% at Day 0 to 5.9% at Day 360 (Fig 1). There is a 34% reduction of HbA1C in Prime patients, while Control patients showed only 3% reduction.

Note: The Freestyle Libre is a device that measures your blood sugar levels continuously for 14 days. Its average MARD (a measure of accuracy) shows that it's usually about 12.8% accurate

Blood Pressure Parameters

2. Systolic Blood Pressure (Sys BP):
Optimum Range: <140 mm Hg

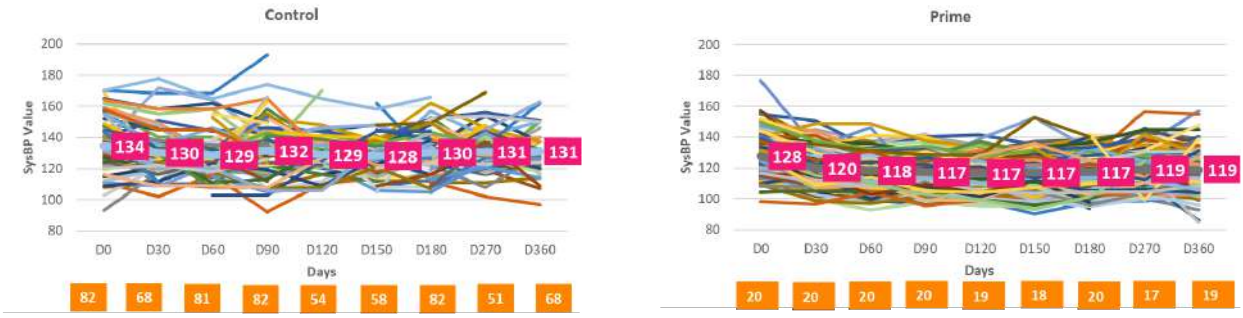


Fig 2 - Change in Systolic Blood Pressure (Sys BP) value from 0th day to 360th days of Control and Prime patients

The mean Systolic BP of the Prime patients decreased from 128 mm Hg at Day 0 to 119 mm Hg at Day 360 (Fig 2).

3. Diastolic Blood Pressure (Dia BP):
Optimum Range: <90 mm Hg

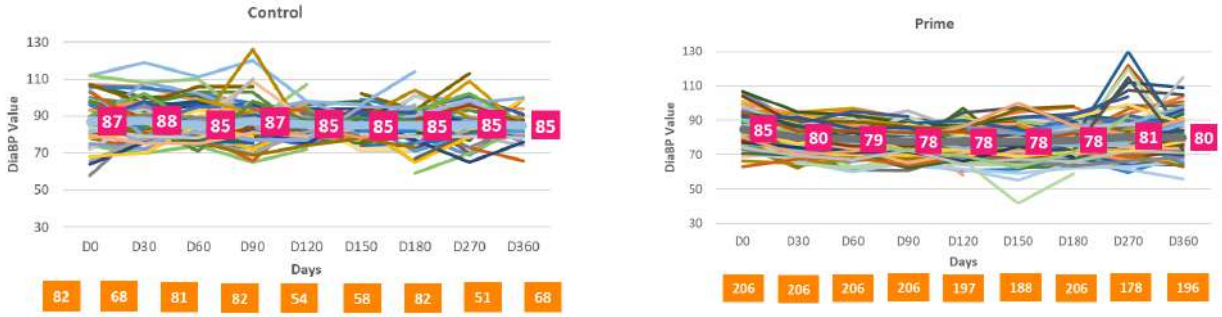


Fig 3 - Change in Diastolic Blood Pressure (Dia BP) from 0th day to 360th days value of Control and Prime patients

The mean Diastolic BP of the Prime patients decreased from 85 mm Hg at Day 0 to 80 mm Hg at Day 360 (Fig 3).

Lipid Parameters

4. Triglycerides:

Triglycerides are a type of fat or lipid that store unused calories. High triglyceride levels (hypertriglyceridemia) are considered a high-risk factor for narrowing of the arteries (atherosclerosis) which can lead to stroke, heart attack, and peripheral arterial disease (PAD).
Optimum Range: <150 mg/dL

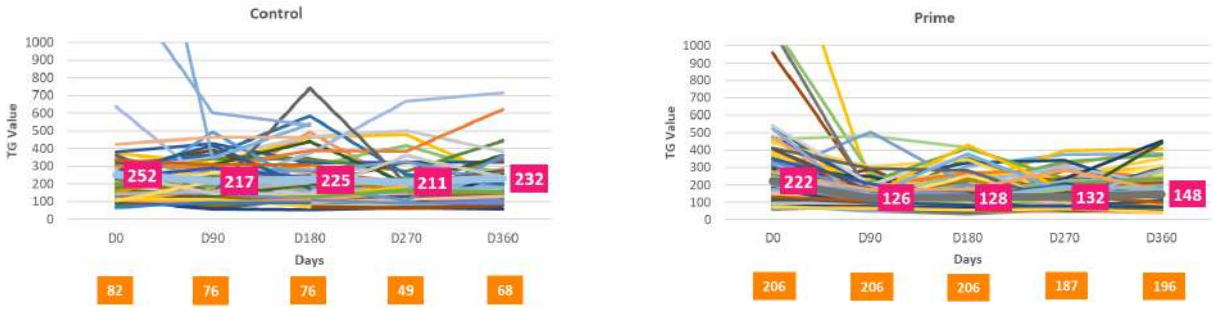


Fig 4 - Change in Triglycerides value from 0th day to 360 days of Control and Prime patients

Mean triglycerides of the Prime patients show a reduction of 33% from 222 mg/dL at Day 0 to 148 mg/dL at Day 360 (Fig 4).

5. Low Density Lipoprotein (LDL):

LDL cholesterol is often called the “bad” cholesterol because it collects in the walls of your blood vessels, raising your chances of health problems like a heart attack or stroke.
Optimum Range: <130 mg/dL

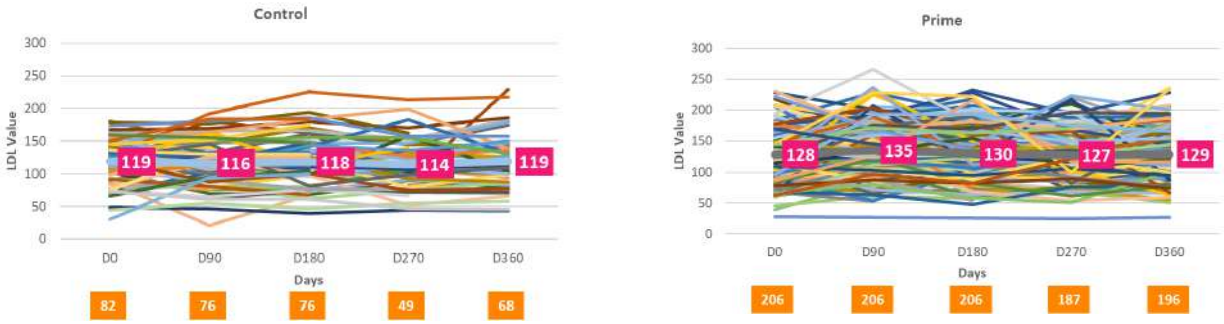


Fig 5 - Change in Low Density Lipoprotein (LDL) value from 0th day to 360th days of Control and Prime patients

53.5% (105/196) of the Prime patients on Day 360 have LDL cholesterol less than 130 mg/dL. (Fig 5)

6. High Density Lipoprotein (HDL):

High Density Lipoprotein (HDL) or “good” cholesterol. HDL takes LDL to your liver, where it i’s flushed out of the body. High HDL levels might protect against heart attacks and strokes.
Optimum Range: >40 mg/dL

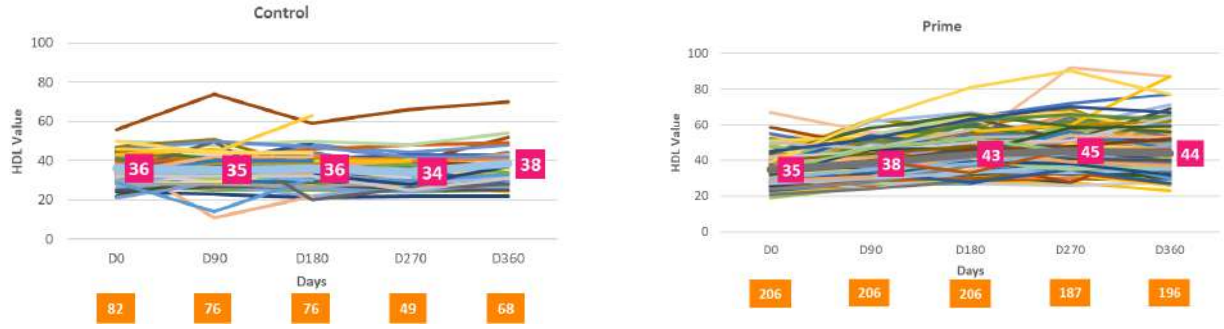


Fig 6 - Change in High Density Lipoprotein (HDL) value from 0th day to 360th days of Control and Prime patients

80.6% (158/196) of the Prime patients have HDL value >40 mg/dL on Day 360 while only 42.6% (29/68) of the Control patients have HDL >40 mg/dL (Fig 6).

Inflammation Parameters

7. High-sensitivity C-Reactive Protein (hs-CRP):

High-sensitivity CRP (hs-CRP) enables a measure of chronic inflammation.
Optimum Range: <3 mg/L

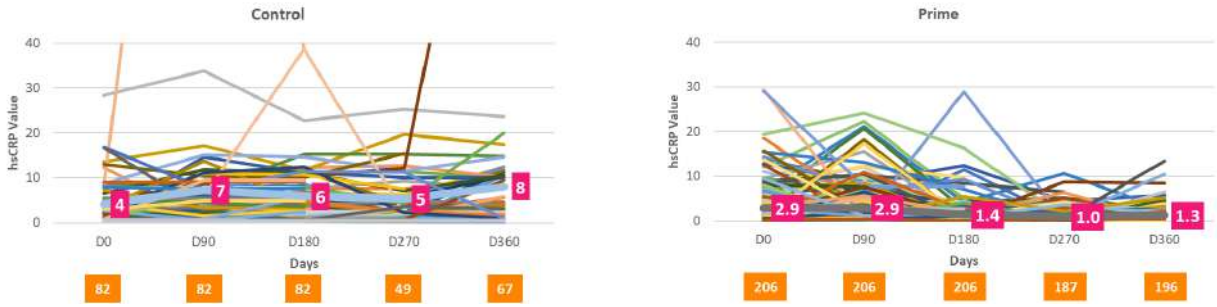


Fig 7 - Change in High-sensitivity C-Reactive Protein (hs-CRP) value from 0th day to 360th days of Control and Prime patients

hs-CRP of Prime patients is highly superior to Control patients. 89.7% (176/196) of the Prime patients have a reduction in the hs-CRP value on Day360 (Fig 7).

Weight Parameter

8. Body mass index (BMI):

Body mass index (BMI) is a measure of body fat based on height and weight.
Optimum Range: <25 kg/m²

Fig 8 - Change in Body mass index (BMI) value from 0th day to 360th days of Control and Prime patients

BMI is controlled better by Prime patients than Control patients. 58.8% (116/197) of the Prime patients have maintained their BMI within the range of <25 kg/m2 on Day 360 (Fig 8).

Atherosclerotic Cardiovascular Disease (ASCVD) 10-Year Risk Score Parameter

The ASCVD (Atherosclerotic Cardiovascular Disease) 10-Year Risk Score is a clinically validated tool used to estimate a patient's 10-year risk of experiencing a cardiovascular event, such as a heart attack or stroke, based on individual risk factors like age, cholesterol levels, blood pressure, diabetes status, and smoking history.
Optimum Range: < 5%

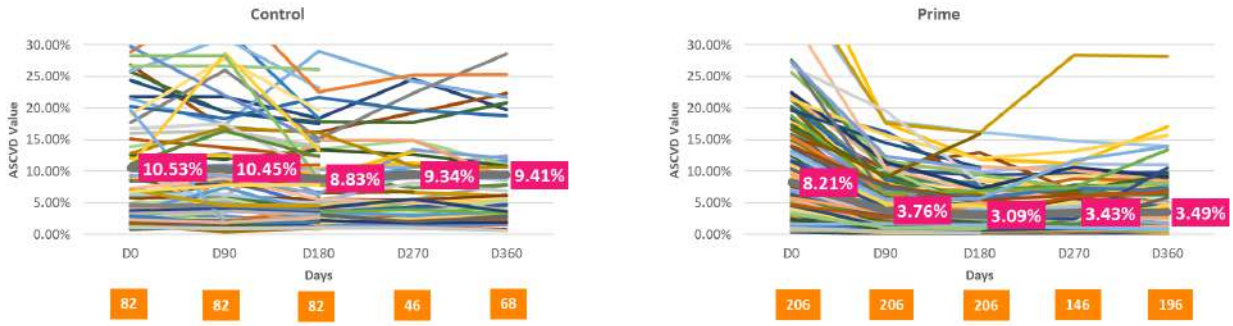


Fig 9 - Change in ASCVD value from 0th day to 360th days of Control and Prime patients

There is a 57.4% reduction in the risk of experiencing a cardiovascular event in Prime patients (Fig 9).

Reduction in the number of patients ASCVD 10-Year Risk Score value

Fig 10 - Reduction in the number of patients ASCVD value from 0th day to 360th days

Note:

ASCVD 10-Year Risk Score (%)	**Risk Category**
< 5%	Low Risk
< 5% to < 7.5%	Borderline Risk
< 7.5% to < 20%	Intermediate Risk
≥ 20%	High Risk

89% of the Prime patients with high-risk score (>20%) have shown reduction in ASCVD value at the end of Day 360 (Fig 10).

B. Examining Recovery Rate of Health Parameters over Time

This recovery analysis shows the rate of transformation of the patient from initial abnormal value to the optimum range and number of days taken to reach there by the individual. The graphs are plotted on the predominant parameters (Diabetic, Blood Pressure, Lipid, Inflammation and Weight parameter).

Represent number of patients at specific days

Represent patients whose health values are in optimum ranges

X Axis – Days of treatment, **Y Axis** – Number of Patients

Diabetic Parameter

1. **Hemoglobin A1C (HbA1C):**
   Optimum Range: <6.5 % with or without Metformin drug

Fig 11 - Hemoglobin (HbA1C) trends of Control and Prime patients

99.5% (205/206) of Prime patients have reached below the optimum range in HbA1C by Day 360 while 25.6% (21/82) of the Control patients have only shown recovery by Day 360 (Fig 11).

Blood Pressure Parameters

2. **Systolic Blood Pressure (Sys BP):**
   Optimum Range: <140 mm Hg

Fig 12 - Systolic Blood Pressure (Sys BP) trends of Control and Prime patients

100% (206) of the Prime patients have shown recovery by Day 360 (Fig 12).

3. Diastolic Blood Pressure (Dia BP):
   Optimum Range: <90 mm Hg

Fig 13 - Diastolic Blood Pressure (Dia BP) trends of Control and Prime patients

100% (206) of the Prime patients have shown recovery by Day 360 (Fig 13).

Lipid Parameters

4. Triglycerides:
   Optimum Range: <150 mg/dL

Fig 14 - Triglycerides trends of Control and Prime Patients

93.6% (193/206) of the Prime patients have reached triglycerides value within the optimum range by Day 360 (Fig 14).

5. Low Density Lipoprotein (LDL):
   Optimum Range: <130 mg/dL

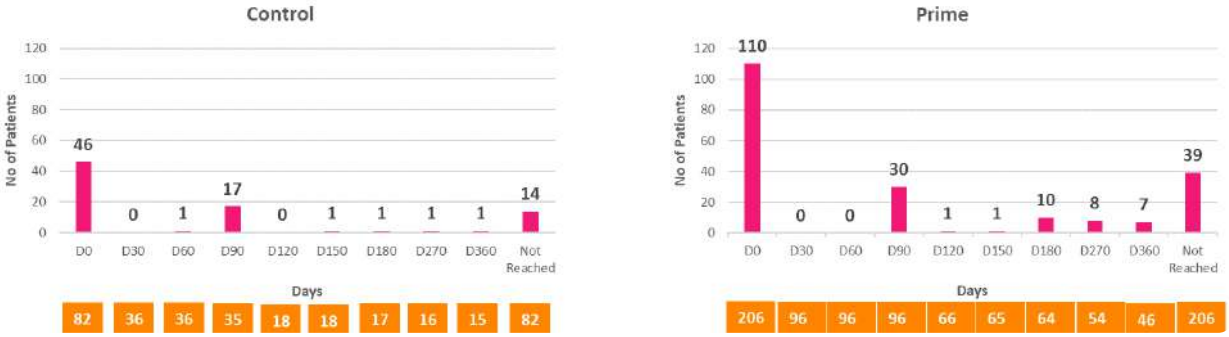


Fig 15 - Low Density Lipoprotein (LDL) trends of Control and Prime patients

81% (167/206) of the Prime patients have reached LDL value within the optimum range by Day 360 (Fig 15).

6. **High Density Lipoprotein (HDL):**
   Optimum Range: >40 mg/dL

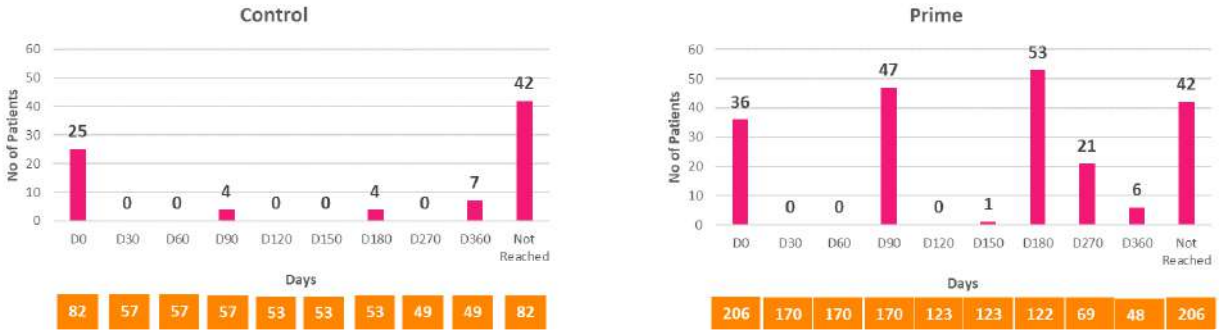


Fig 16 - High Density Lipoprotein (HDL) trends on Control and Prime patients

79.6% (164/206) of the Prime patients have reached HDL value within the optimum range by Day 360 (Fig 16).

Inflammation Parameter

7. **High-sensitivity C-Reactive Protein (hs-CRP):**
   Optimum Range: <3 mg/L

Fig 17 - High-Sensitivity C-Reactive Protein (hs-CRP) trends of Control and Prime patients

98.5% (203/206) of Prime patients have reached below the optimum range in hs-CRP by Day 360 while 69.5% (57/82) of the Control patients have only shown recovery by Day 360 (Fig 17).

Weight Parameters

8. **Body mass index (BMI):**
   Optimum Range: <25 kg/m²

Fig 18 - Body Mass Index (BMI) trends of Control and Prime patients

75.2% (155/206) Prime patients have shown optimum BMI range by Day 360 (Fig 18).

C. Assessing Reduction in Patient's Medication Usage

The analysis shows the comparison for change in the consumption of anti-diabetic medications and not taking any medicine at 0, 30, 60, 90, 120, 150, 180, 270, 360 days across all the Control and Prime patients.

Represent number of patients data available on specific days

X Axis – Days of treatment, **Y Axis** – Number of Patients

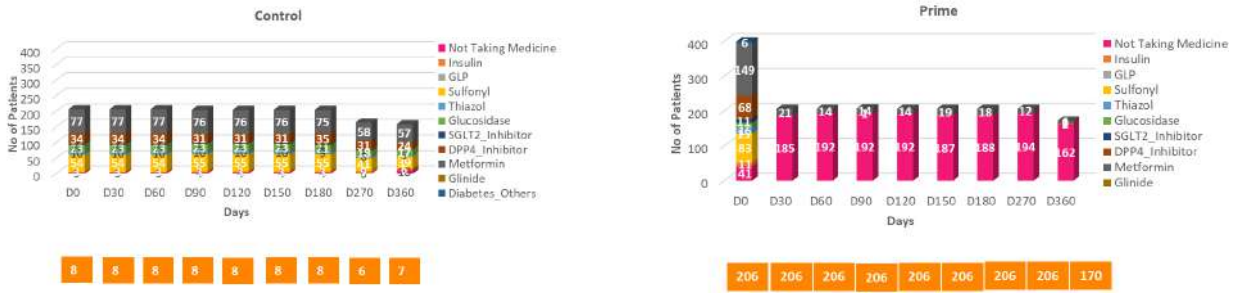


Fig 19 - Change in the patients taking medications for Type 2 diabetes from 0th day to 360th days.

The Prime program has achieved these results with having over 90% taking zero medications from Day 30 itself (Fig 19).

All Prime patients who were on insulin, metformin, DPP-4 inhibitors, alpha-glucosidase inhibitors, sulfonylureas, or sodium - glucose cotransporter-2 (SGLT2) inhibitors at baseline, were able to stop taking these medications within 1 month of starting the program.

D. Correlation between Food Consumption and Health Metrics

Foods are categorized as "Green, Orange or Red" based on the post-meal glucose spikes. Green foods are those which produces post-meal glucose AUC value less than 70. Orange foods are those which produces post-meal glucose AUC value between 70 and 100. Red foods are those which produces post-meal glucose AUC value greater than 100. Hence foods with high post-meal glucose AUC are considered as Red foods and are not tolerated by the individual's metabolism.

Food Colors	Post meal Glucose AUC value	Food Rating
Green (Must eat)	< 70	> 2 to 3
Orange (Good to eat)	70 - 100	> 1 to 2
Red (Must not eat)	> 100	0 to 1

Formulation:

$$\text{Food Rating} = \mathbf{3} - \frac{AUC}{70} \text{ if AUC} < 70; \mathbf{max}\left(\mathbf{2} - \frac{(AUC - 70)}{30}, \mathbf{0}\right) \text{ if AUC} >= 70$$

Engagement score: Member opened the App at least once during the day and had at least one sensor feed data.

Sensors include a sensor watch (Fitbit Charge 2®) to track activity and resting heart rate, a smart body composition scale (Powermax® BCA-130 Bluetooth Smart Scale), and an arm blood pressure meter (TAIDOC® TD-3140).

Adherence score: Member logged at least one Green meal and used at least one sensor.

Sensors include a sensor watch (Fitbit Charge 2®) to track activity and resting heart rate, a smart body composition scale (Powermax® BCA-130 Bluetooth Smart Scale), and an arm blood pressure meter (TAIDOC® TD-3140).

Hemoglobin A1C (HbA1C): (Optimum Range: <6.5 % with or without Metformin drug)

HbA1C represents the Glycated Hemoglobin. HbA1c depicts the last 2-to-3-month average blood glucose.

Metabolic score: (Optimum Range: >80)

Includes 10 metabolic health markers (Diabetes Score, Blood Pressure Score, Dyslipidemia Score, Obesity Score, Liver Score, Kidney Score, Pancreas Score, Heart Score, Insulin Resistance Score, Inflammation Score) that involves sensor data and lab work.

100 Randomized Controlled Trials (RCT) patients have been considered for reference during their treatment period starting from April 2021 to June 2022.

Individual Patient's Food Analysis

The food analysis establishes the correlation between foods consumed by the individual patient with HbA1C value, Metabolic Score, Engagement score, and Adherence score.

Patient 1

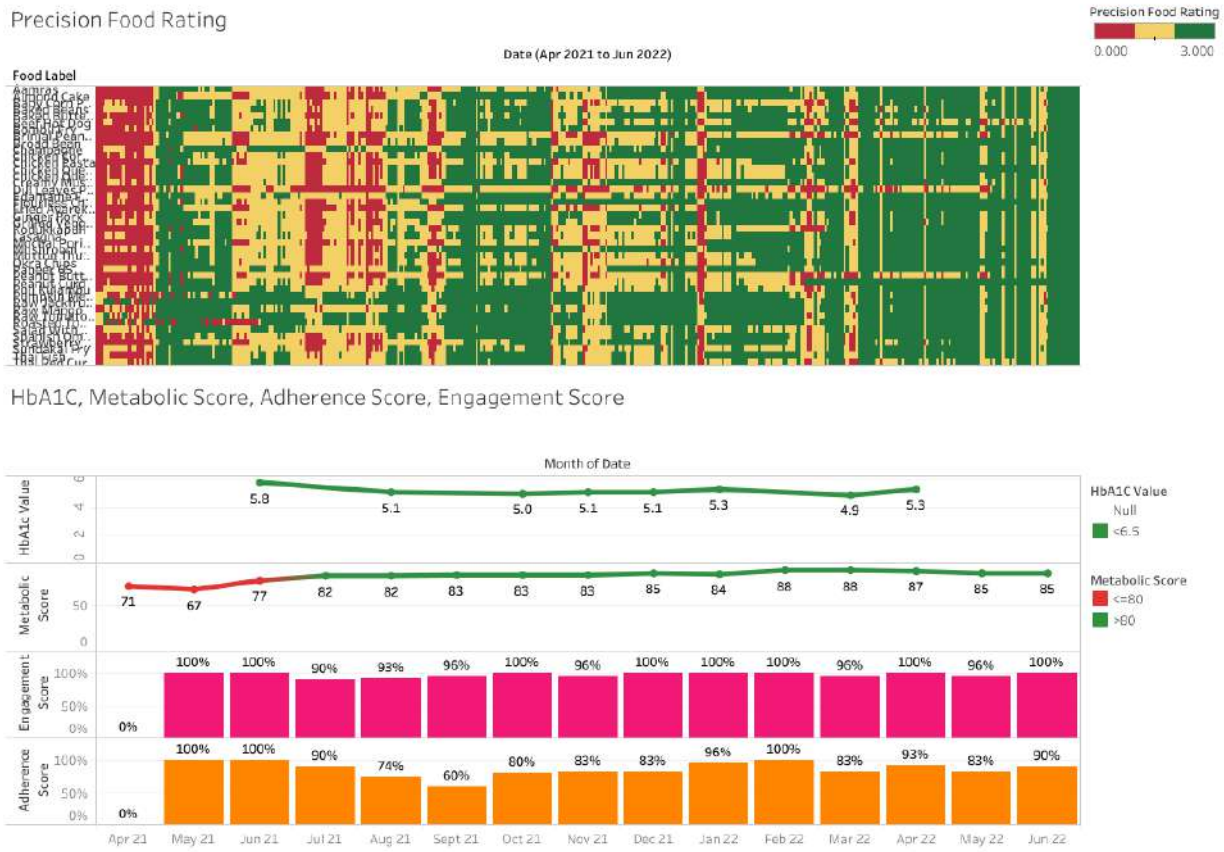


Fig 20 - Food transformation from red to green with HbA1C value, Metabolic score, Engagement score and Adherence score.

As the HbA1C and Metabolic Score reach an optimal range, a significant portion of the food shifts to the green category. Engagement score and Adherence score is stable throughout the treatment period.

Patient 2

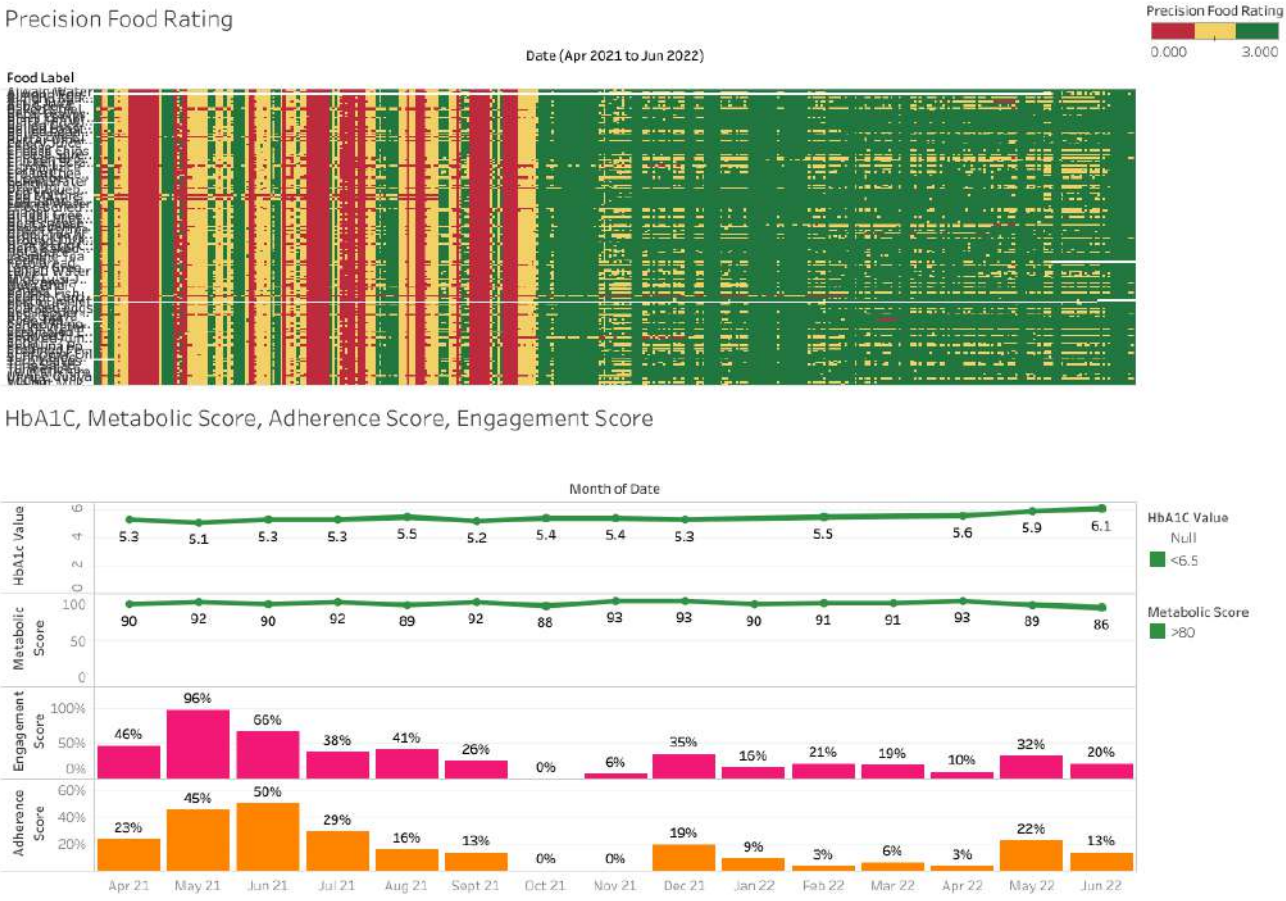


Fig 21 - Food transformation from red to green with HbA1C value, Metabolic score, Engagement score and Adherence score.

Throughout the treatment period, the HbA1C and Metabolic Score consistently remain within the optimum range, indicating a successful transformation from red food to green food. In contrast, while the HbA1C remains within the normal range, the Engagement score and Adherence score show inconsistency throughout the treatment period.

Patient 3

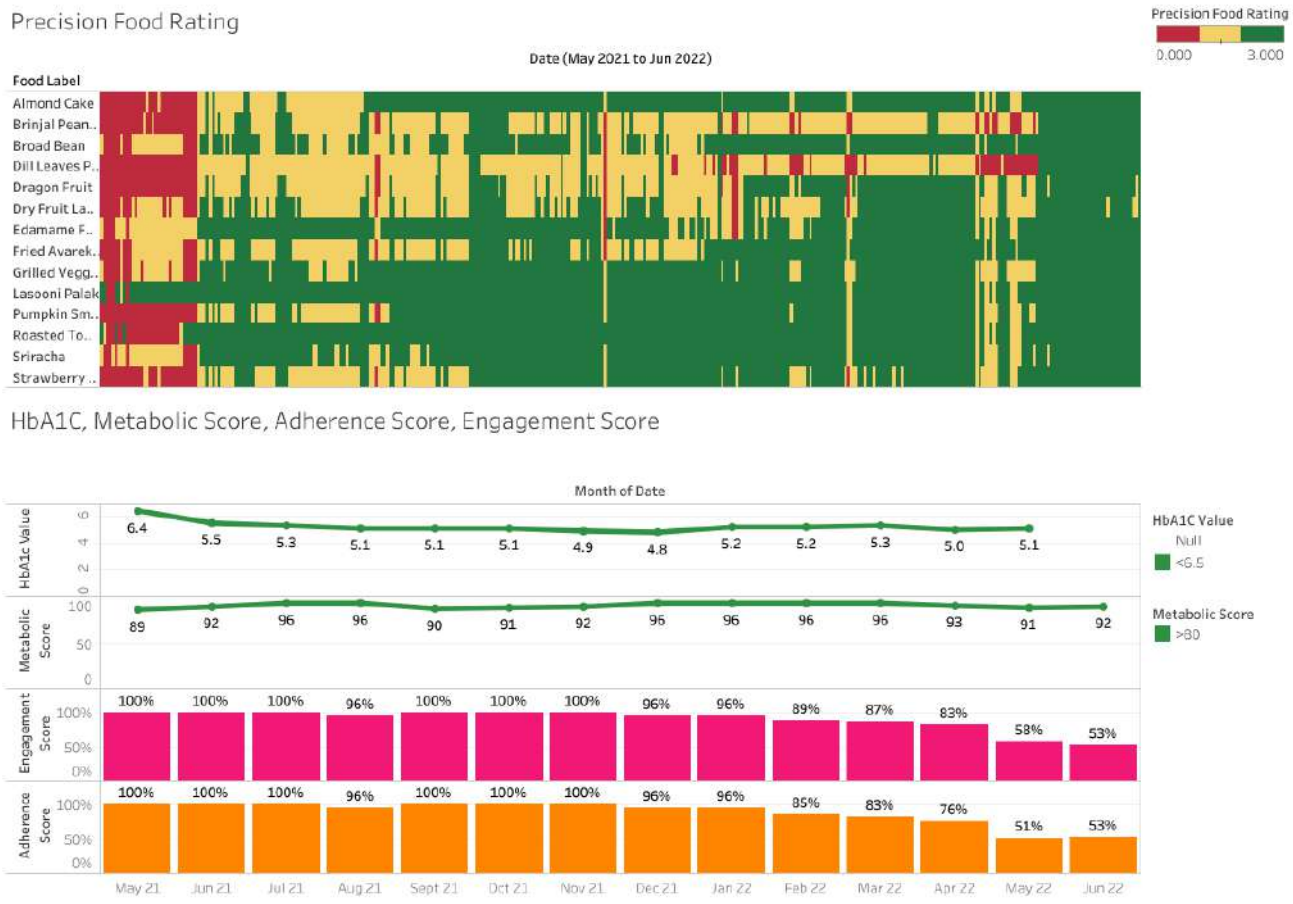
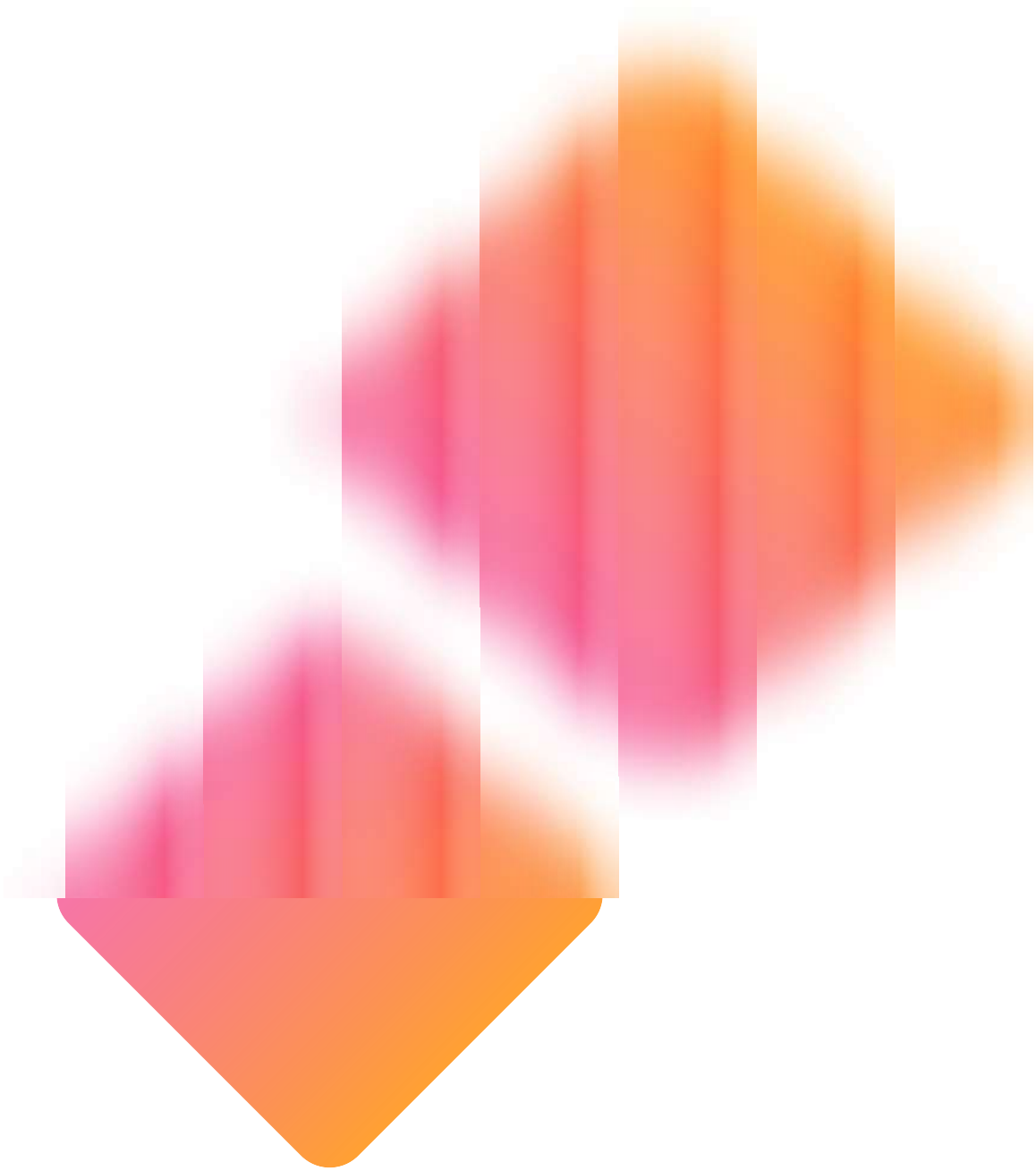


Fig 22 - Food transformation from red to green with HbA1C value, Metabolic score, Engagement score and Adherence score

With the HbA1C and Metabolic Score at optimal levels, a significant portion of the food is categorized as green. The Engagement score and Adherence score remain consistent throughout the treatment duration, although there is a slight decrease in engagement and adherence in the last two months.

Inference:

Patients who engaged and adhered to the Twin Precision Nutrition Program (TPN) for 1 year have shown optimum values for post-meal glucose AUC values and metabolic score displaying results of Red to Green transformations.
(Fig 20, Fig 21, Fig 22).



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