Controlling Obesity-Associated Comorbidities through Weight Loss

## Genetics and Gut Microbiome-based Precision Medicine

Abstract

As obesity rates skyrocket in the United States, the landscape of American healthcare is changing.

The medical system is faltering under the exponentially rising costs of managing obesity-related metabolic illnesses and comorbidities such as diabetes, cardiovascular disease, and mental health. Personalized nutrition, leveraging the power of genetic and microbiomic information that can now be sampled on an individual basis, is altering clinicians' capacity to effect weight loss in patients. Digbi Health, a precision digital care platform, offers a program leveraging participants' unique Genetics and gut microbiome profiles along with an app and personalized health coaching to manage healthy and sustainable weight loss.

A survey of individuals who were able to lose at least 5% of their starting body weight within 100 days of commencing the Digbi Health program identified significant reduction in presentation of comorbidities - namely three of the most physically and financially debilitating obesity-related comorbidities: Cardiovascular Hypertension, Diabetes and Gastrointestinal Disease.

Introduction

DIABETES

HYPERTENSION

GASTROINTESTINAL DISEASE
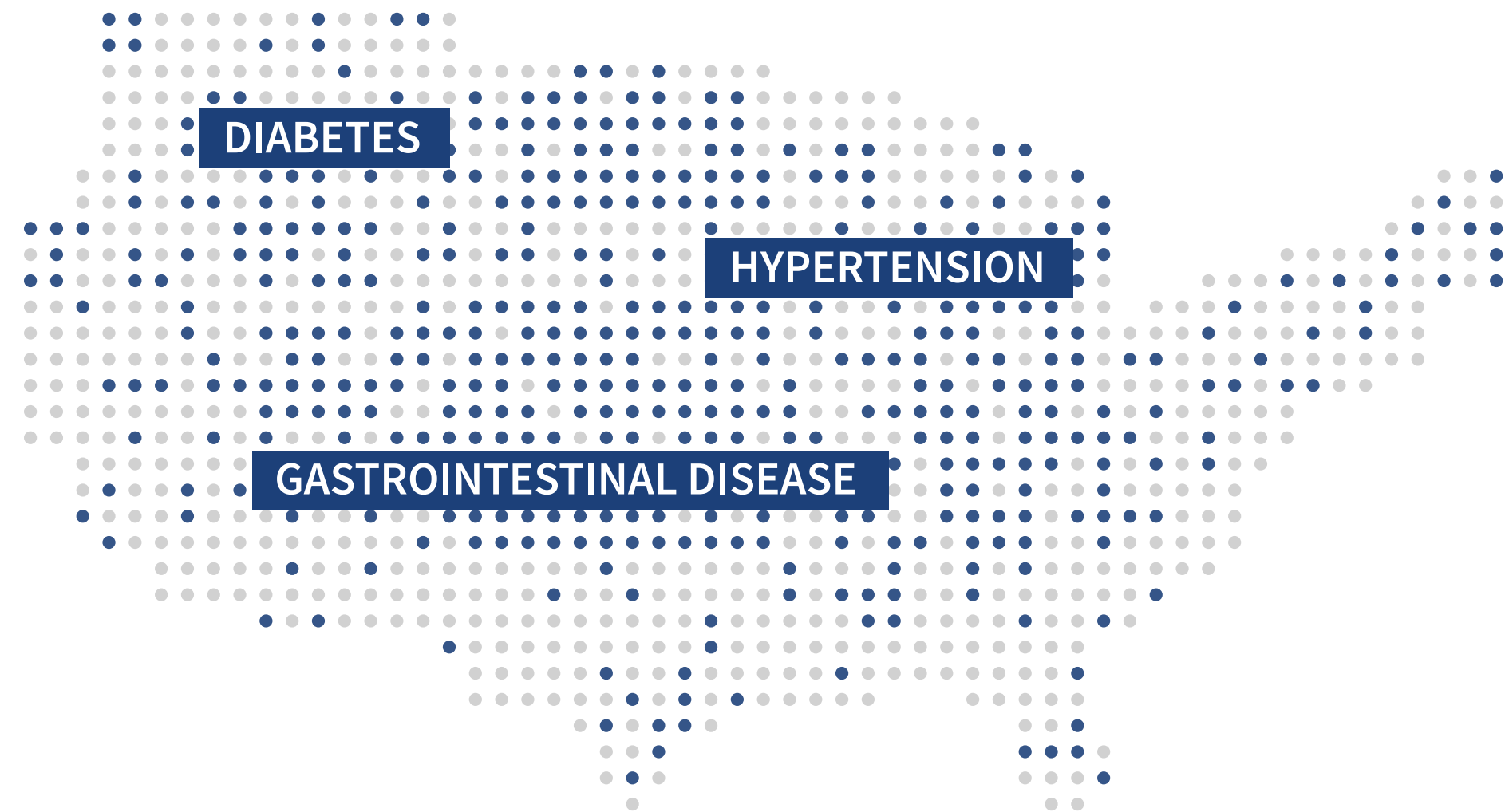
The global obesity epidemic presents a major public health concern as the prevalence of obesity in the U.S. has increased substantially from the early 1960s, when a little over 10% were obese, to now almost 40% - over 60 million adults. [1, 2] Although a precise cause of obesity has yet to be discovered, several factors have been linked to its development.[3] In particular, biological factors interact with behavioral factors and demographic influences such as socioeconomic status, or even cuisine, to influence obesity risk.[4] Obesity-associated biological factors include, but are far from limited to, genetics and epigenetics, microbiomic composition, age, circadian rhythm disruption, pharmaceutical interactions, and co-morbidities and their management.[4, 5]

Three notable comorbidities, themselves with serious health implications indicative of the current health landscape in the United States, are hypertension (high blood pressure), insulin-related illness (namely pre-diabetes and Type II, non-insulin dependent, diabetes), and gastrointestinal disease.[6] All three of these comorbidities experience demonstrable reduction upon weight loss.[7, 8, 9]

With all these comorbidities, more weight loss produces more improvement, but even just moderate weight loss (5–10%) is associated with reduction in health care costs.[8] Subjects who lose between 5% to 10% of their initial body show the same reduction in blood pressure as those who undergo an intensive yearlong lifestyle management program.[7] Even just 5-7% - can prevent progression of impaired glucose tolerance (pre-diabetes) into Type 2 Diabetes.[8] Weight loss even has implications for gastric health - in one study, 5-10% weight loss was associated with an 8% reduction in prevalence of IBS.[9]

Diabetes

01

30 MIL +
of the U.S. population, suffer from diabetes

More than 30 million adults, almost 10% of the U.S. population, suffer from diabetes.[10] A further 84 million American adults (more than a third of the population) are suspected to suffer from pre-diabetes.

In 2014, there were more than 14 million emergency room visits and 7 million hospitalizations linked to insulin-related illness - the disease is of major public health concern costing close to $250 billion in annual health expenditures.[10]

Furthermore, only about a quarter of those who have successfully completed a calorie restrictive weight loss program such as Weight Watchers are able to maintain their full weight loss for a year beyond program completion; in fact, more than 20% of Weight Watchers participants are unable to maintain even 5% of their weight loss beyond a year.[13]

The diagnosis and progression of pre-diabetes and Type 2 (non-insulin dependent) diabetes (T2D) are skyrocketing in the U.S., indicating a need for novel approaches to halting the progression of these diseases.

The current standard of care for pre-diabetics (per the Centers for Disease Control and Prevention) involves a "one size fits all" approach to increasing physical activity and decreasing caloric and glycemic intake while undergoing a year-long lifestyle coaching program.[11] Only about 40% of those who have successfully completed an intervention such as the CDC's "Prevent T2" program are able to lose 5% or more of their body weight in that year.[12]

Digestive Disorders

02

Digestive diseases related to obesity include gastroesophageal reflux disease (GERD), as well as its progression into Barrett's esophagus and esophageal cancers; other carcinomas such as colon polyps and cancers, cholangiocarcinomas, pancreatic cancers, and hepatocellular carcinomas; other liver-related ailments such as nonalcoholic fatty liver disease and hepatitis C-related disease; and gallstones. Diseases such as these annually affect more than 60 million Americans.[14] Every year, gastrointestinal ailments are associated with close to 5 million hospitalizations, more than 70 million ambulatory care visits, over 200,000 deaths, and close to $150 billion dollars in direct and indirect costs.[14]

Recent research has elucidated the relationship between commensal gut microbiota and a spectrum of digestive disorders, primarily via modulation of inflammatory pathways.[15]

Microbial diversity has been shown to be a hallmark of gut health, and perturbations to the microbial environment, especially those that result in reduced diversity are commonly known as gut dysbiosis; dysbiosis, in turn, is shown to be related to a variety of gastric conditions including chronic Irritable Bowel Syndrome and diarrhea.[16]

Recent evidence indicates that management of both obesity as well as gut microbiome to alleviate dysbiosis can be instrumental in improving gastrointestinal health.[15]

OBESITY	GUT BIOME

GASTROINTESTINAL HEALTH
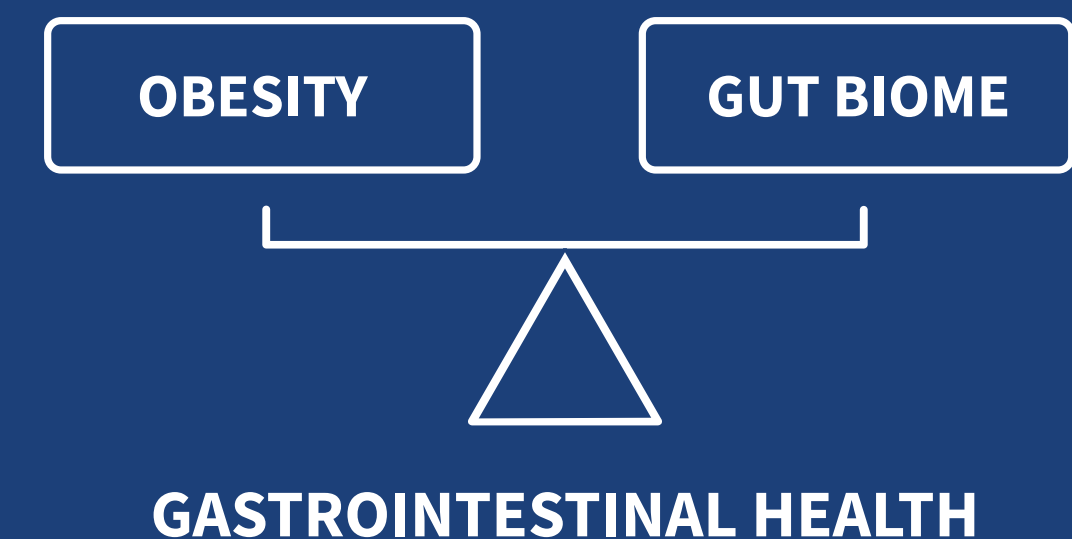
Hypertension

03

Epidemiological studies have shown a correlation between body weight and blood pressure in obese populations.[17] Although the relationship between obesity and hypertension is well established in children and adults, the mechanism by which obesity directly causes hypertension is sometimes poorly understood.[18]

Obesity accounts for 65-75% of hypertension risk, and research has clearly established that BMI and blood pressure are directly proportional to one another.

65-75%
HYPERTENSION RISK

In fact, an obese individual tends to have a higher blood pressure than would an otherwise identical person but for a lower body weight. [17]

Hospitalizations due to primary and secondary hypertension more than doubled since the 1970s and 80s, and the attendant annual costs have risen from $40 billion in the early 80s to $113 billion (15.1% of total hospital costs) in the mid 00s.[19] Today, a third of American adults suffer from hypertension,[19] and although that number stabilized somewhat in the last two decades, [20] the estimated number of years of life lost to hypertension-related diseases in 2010 included: ischemic heart disease 7.2 million; stroke 1.9 million; chronic kidney disease, other cardiovascular and circulatory, and hypertensive heart disease 2.2 million combined.[20]

Materials & Methods
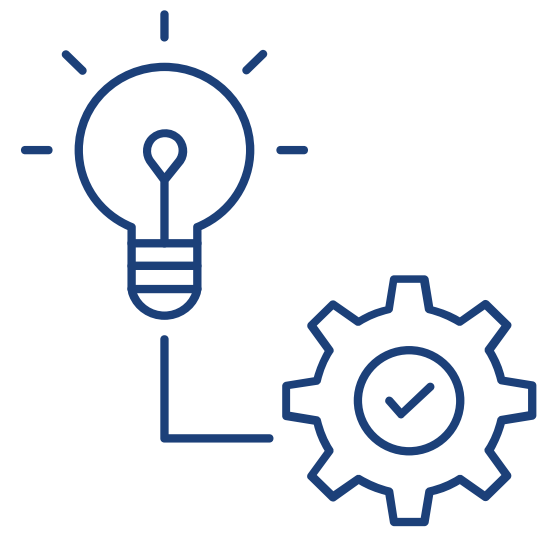
The Digbi Health programs are geared primarily toward individuals who are overweight or obese, with or without comorbidities, and functions as a weight loss and management tool including personalized health coaching coupled with curated nutritional and lifestyle recommendations based upon one's individual genetic and microbiomic profiles.

According to the World Health Organization (WHO), "overweight" and "obese" are defined as having abnormal or excessive fat accumulation that presents a risk to health, including diabetes and cardiovascular disease. [21]

The National Heart, Lung, and Blood Institute (NHLBI) defines a body mass index (BMI) of more than 25 as overweight, a BMI above 30 as obese, and a BMI above 40.9 as severely obese. [22]
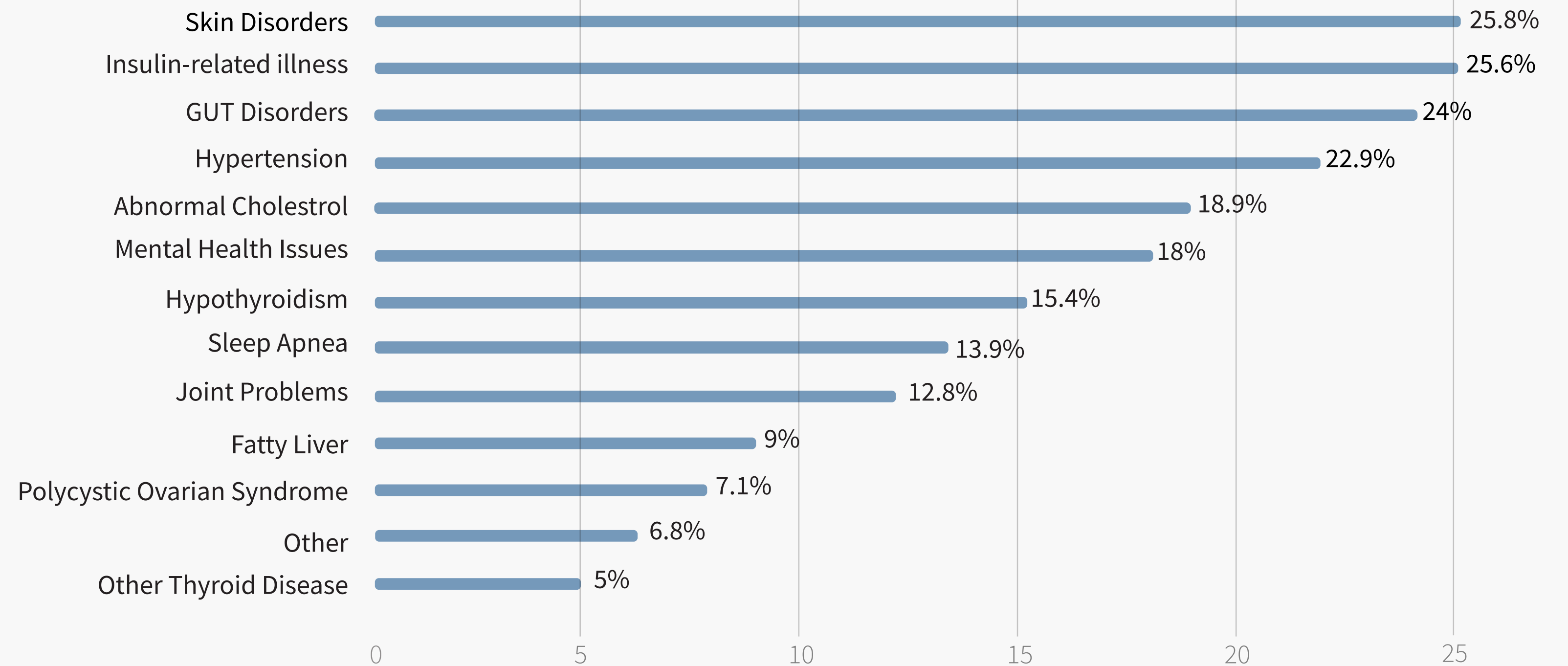
Digbi Health users with comorbitities reported

Of the overweight and obese individuals utilizing the Digbi Health program:
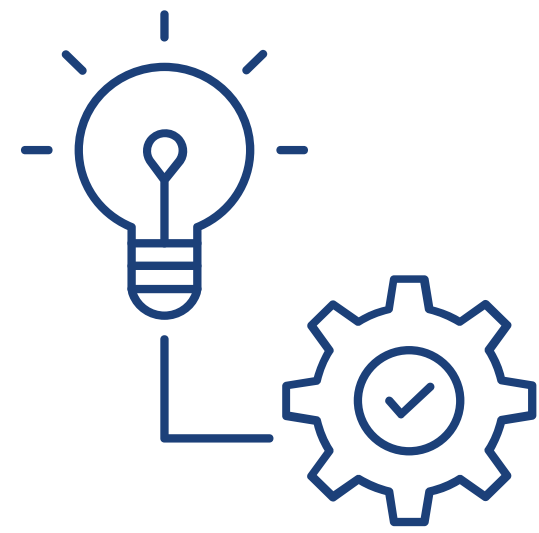
24%
suffer from digestive disorders

25.6%
suffer from insulin-related illnesses (pre-diabetes, gestational diabetes, Type I and II Diabetes)

25.8%
suffer from concurrent skin-related comorbidities

22.9%
suffer from hypertension

Condition	Percentage
Skin Disorders	25.8%
Insulin-related illness	25.6%
GUT Disorders	24%
Hypertension	22.9%
Abnormal Cholestrol	18.9%
Mental Health Issues	18%
Hypothyroidism	15.4%
Sleep Apnea	13.9%
Joint Problems	12.8%
Fatty Liver	9%
Polycystic Ovarian Syndrome	7.1%
Other	6.8%
Other Thyroid Disease	5%

Materials & Methods

The Digbi Health program is a 24-week program that uses body metrics, gut microbiome and genetic profiles, and personalized health-coaching to deliver a weight loss program.
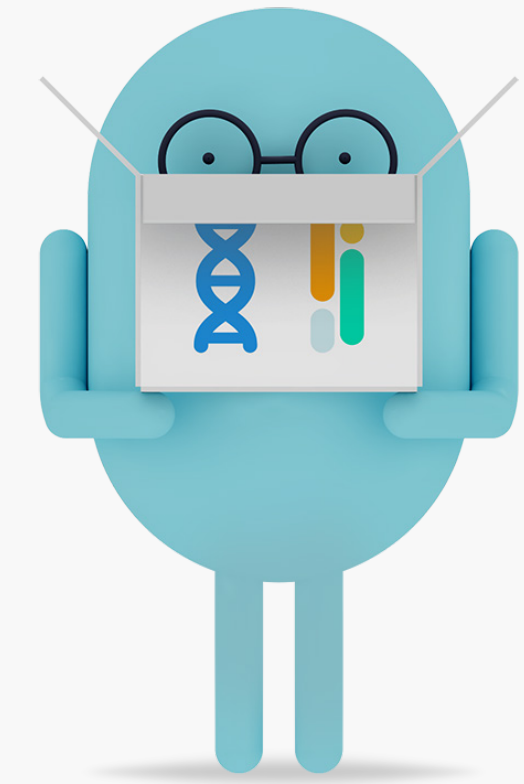
Participants use the Digbi Health app to track 10 key lifestyle and wellness markers (weight, sleep, hunger, cravings, stress, meditation, superfoods, morning energy, foods to avoid and exercise) on a daily basis, take photos of the food they consume, and are assigned a health coach who works personally with the participant through 12 guided sessions at various intervals to interpret personalized wellness reports generated from sampling participants' genes and gut microbiota. The reports also provide a breakdown of obesity risk based on an individual's genetic and gut microbiome profiles. The program is geared toward participants losing at least 5% of their starting body weight by week 16 of the 24-week program.

In this analysis, a group of Digbi Health participants who achieved at least 5% weight loss within 100 days were surveyed to determine if they showed an improvement in any of their comorbidities' symptoms. Forty-five individuals responded to the survey, and here are the results.
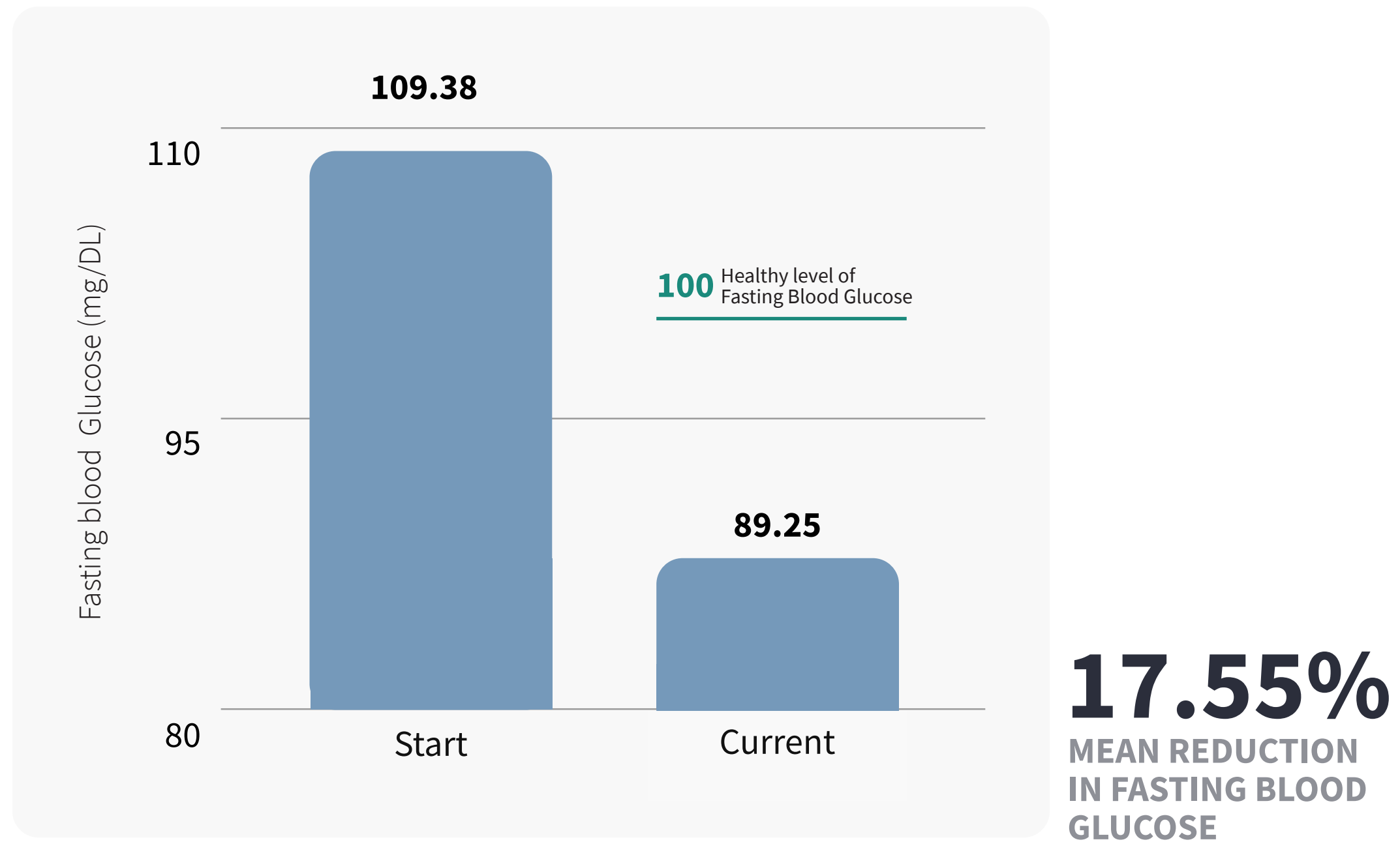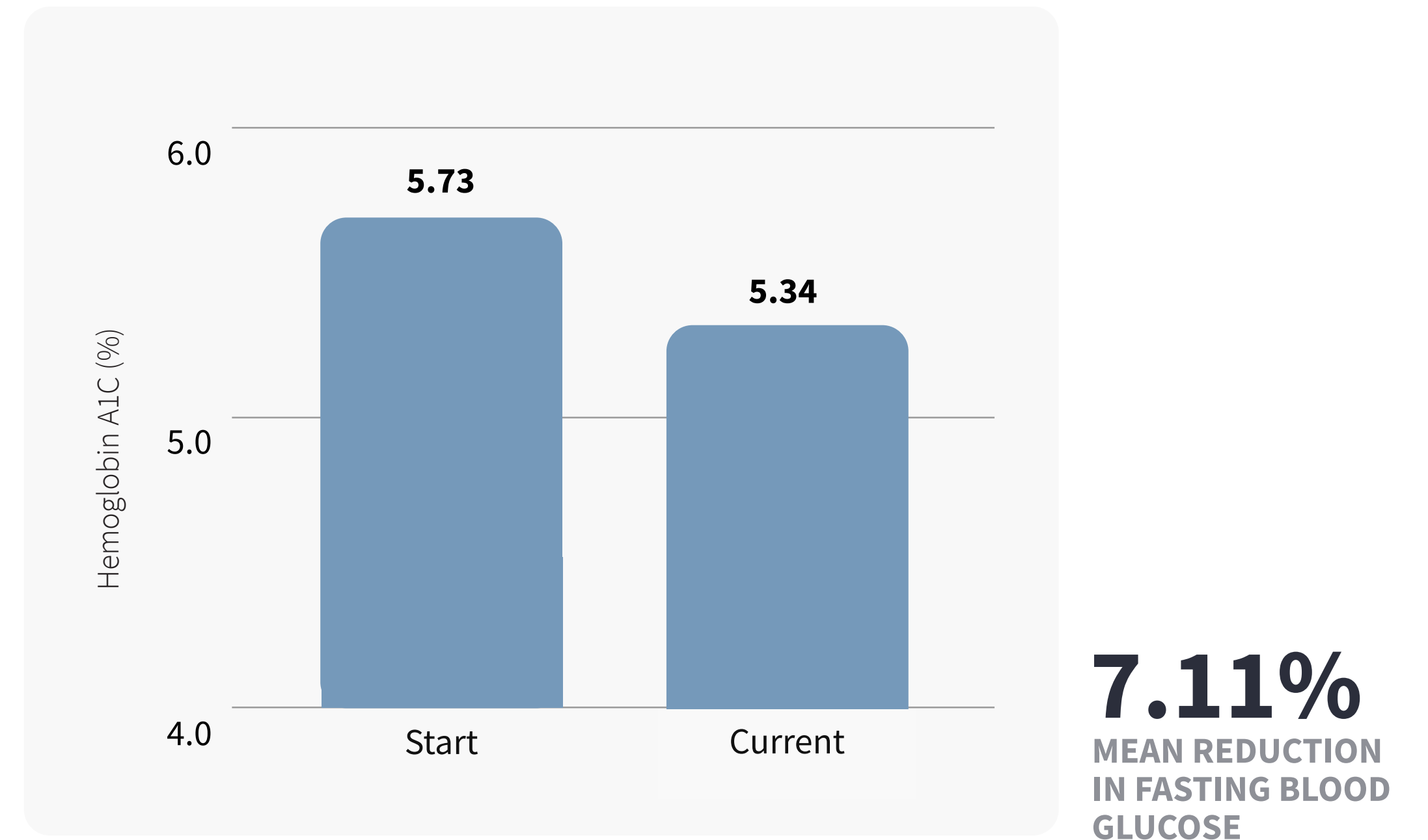
Results

Weight loss with Digbi Health
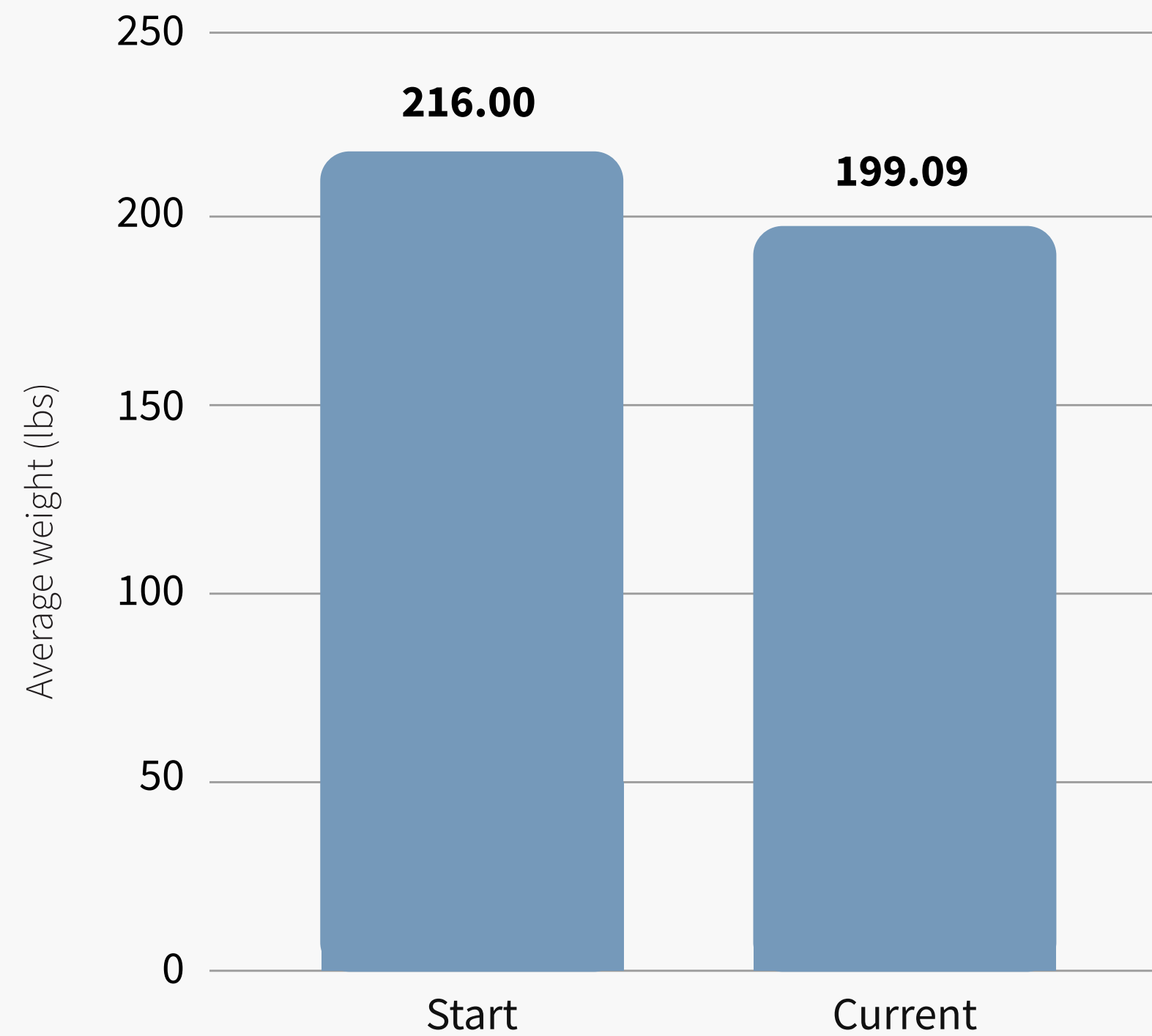
8.23% MEAN WEIGHT LOSS

In the cohort of 45 individuals who both lost at least 5% of their starting bodyweight within 100 days and responded to the follow-up survey, the mean starting bodyweight was 216 lbs, the mean current body weight is 199.09 lbs, and individuals lost, on average, approximately 8.23% of their starting weight.

Blood Sugar and Hemoglobin A1C

Blood Sugar (fig. A)

- 109.38 (Start)
- 89.25 (Current)
- 100 Healthy level of Fasting Blood Glucose
- Fasting blood Glucose (mg/DL)

17.55%
MEAN REDUCTION IN FASTING BLOOD GLUCOSE

Hemoglobin A1C (fig. B)

- 5.73 (Start)
- 5.34 (Current)
- Hemoglobin A1C (%)

7.11%
MEAN REDUCTION IN FASTING BLOOD GLUCOSE

Participants with self-reported insulin-related illness (pre-diabetes or Type II Diabetes) experienced significant alleviation of diabetic symptoms. At the **start** of the program, participants had a mean **fasting blood glucose level of 109.38 mg/dL and a mean HbA1c percentage of 5.73**. At the time of **survey completion**, the same cohort had a **mean fasting blood glucose level of 89.25 mg/dL** (average 17.55% reduction per participant) **and a mean HbA1c percentage of 5.73** (average 7.11% reduction per participant) (Figs A and B).

Gastrointestinal symptoms
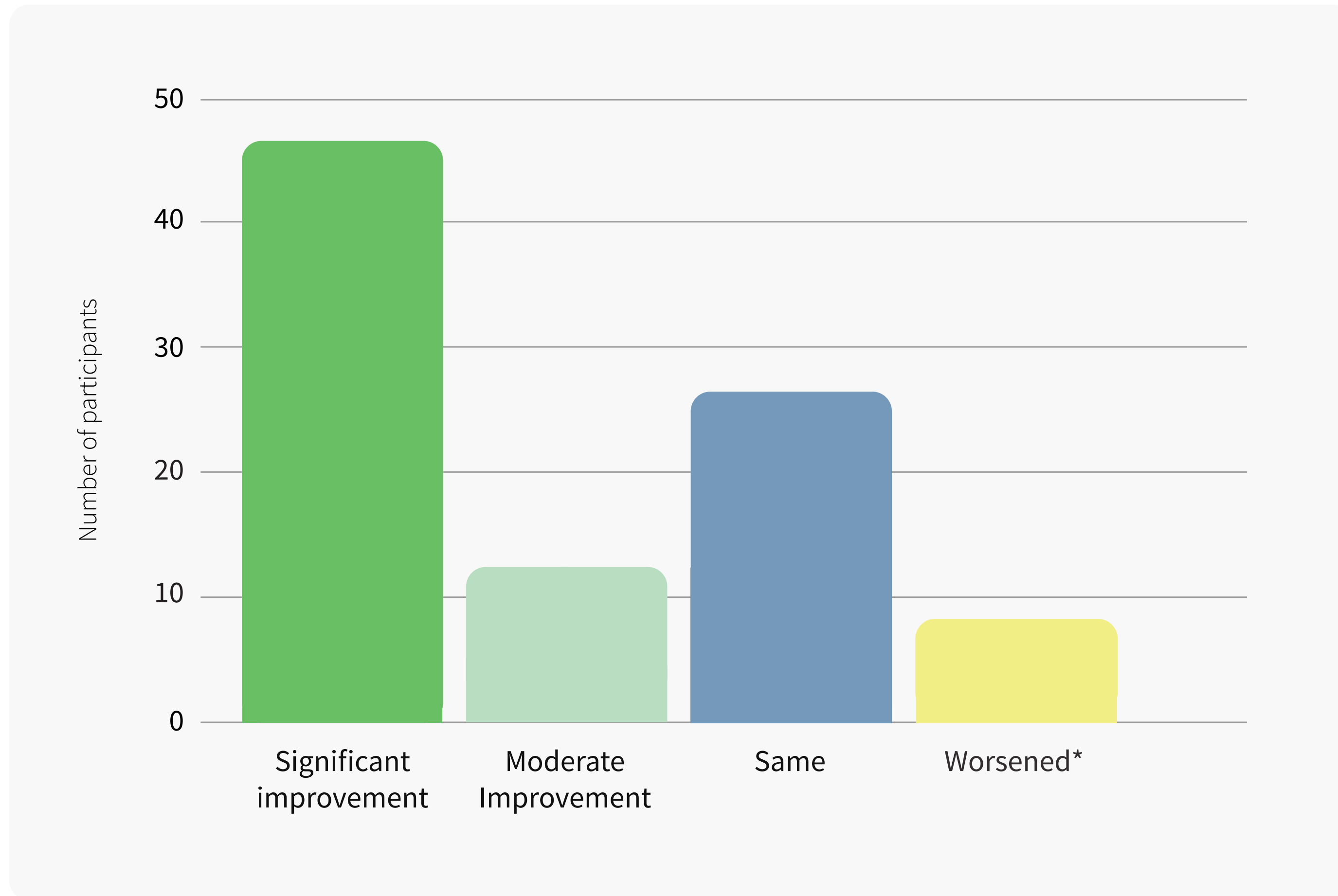
Number of participants

50
40
30
20
10
0

Significant improvement | Moderate Improvement | Same | Worsened*

A majority of survey participants self-reported significant improvement of gastrointestinal symptoms upon participating in the Digbi Health program:

60% +
reported some improvement in symptoms

46.3%
reported significant improvement

● Significan improvement   ● Moderate Improvement   ● Same   ● Worsened

* these results may vary from person to person and some patients may see worsening of symptoms

Gastrointestinal symptoms subtypes

Number of participants

40
30
20
10
0

IBS Bloat GERD Gas Pain Constip Diarr

● Significant improvement   ● Moderate Improvement   ● Same   ● Worsened*
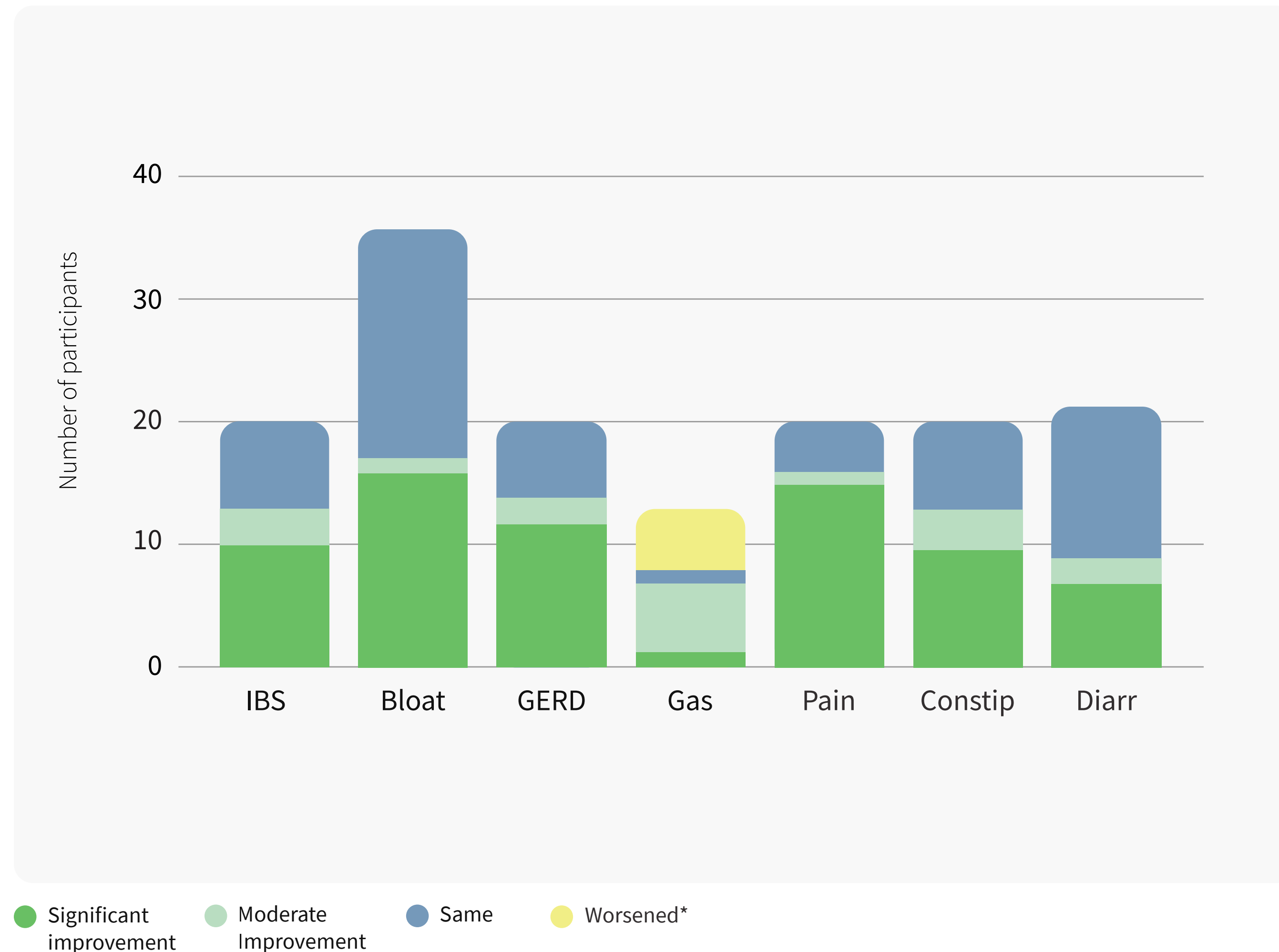
When looking at the various subtypes of gastrointestinal symptoms:

• Greatest improvements were seen in **gastric pain - 75% of respondents experienced significant reduction in pain whereas only 20% experienced no change** (and none experienced an increase).

• In fact, of the various measures of gastrointestinal distress, only sufferers of gassiness experienced an increase in symptoms - **46% experienced more gas during the program than before it** (although the same percentage experienced some relief).

• With regard to gas, these symptoms are likely a function of significantly increased dietary vegetable/fiber intake and could be relieved with better hydration.

• Irritable Bowel Syndrome, gastroesophageal reflux, gastric pain, and constipations all had more respondents reporting symptom improvement compared with symptoms remaining the same.

• **50% of respondents suffering from abdominal bloating experienced improvement** (94% of them experiencing significant improvement).

• **The majority of diarrhea sufferers saw no change in symptoms, but almost 41% did improve** (78% of them significantly).

* these results may vary from person to person and some patients may see worsening of symptoms

Blood Pressure
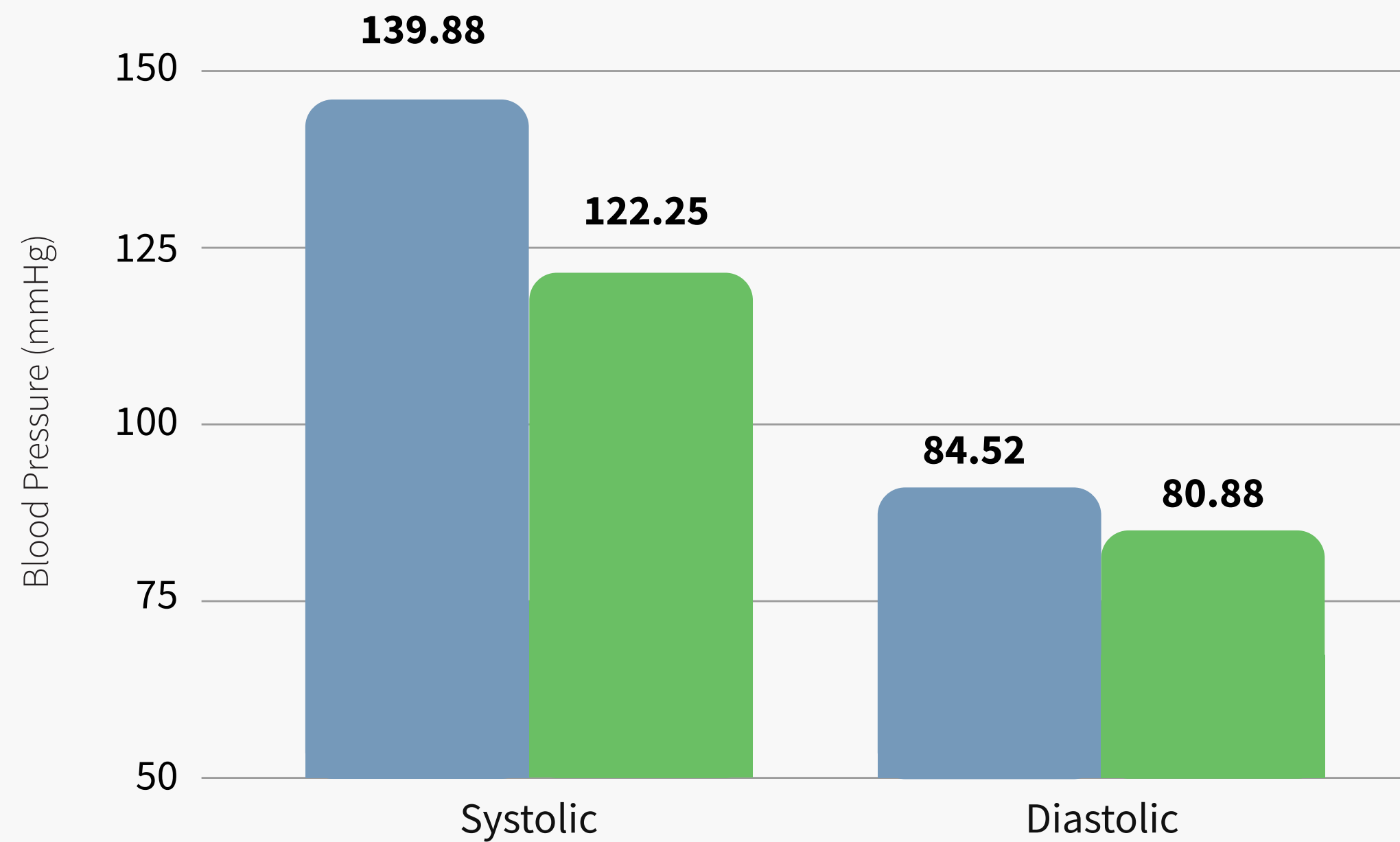
9.92%
MEAN REDUCTION IN SYSTOLIC BLOOD PRESSURE

4.31%
MEAN REDUCTION IN DIASTOLIC BLOOD PRESSURE

Blood pressure of hypertensive participants improved on the program with a smaller difference seen in diastolic blood pressure than in systolic. Participants experienced 9.92% mean reduction in systolic blood pressure and 4.31% mean reduction in diastolic blood pressure.

Digbi Health Delivers RESULTS that matter
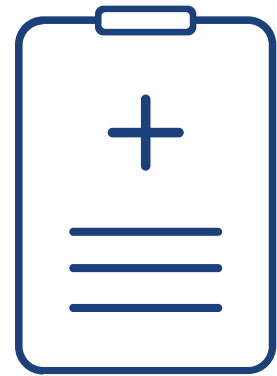
8.92%
Reduction in Weight

6.73%
Reduction in
HbA1C levels

80%
Remission or reduction
in GUT symptoms, IBS
Acid Reflux

66%
Remission or reduction
of Chronic Pain

75%
Reduction of
Headaches/Migraines

50%
Remission or reduction
of Sleep Apnea

22%
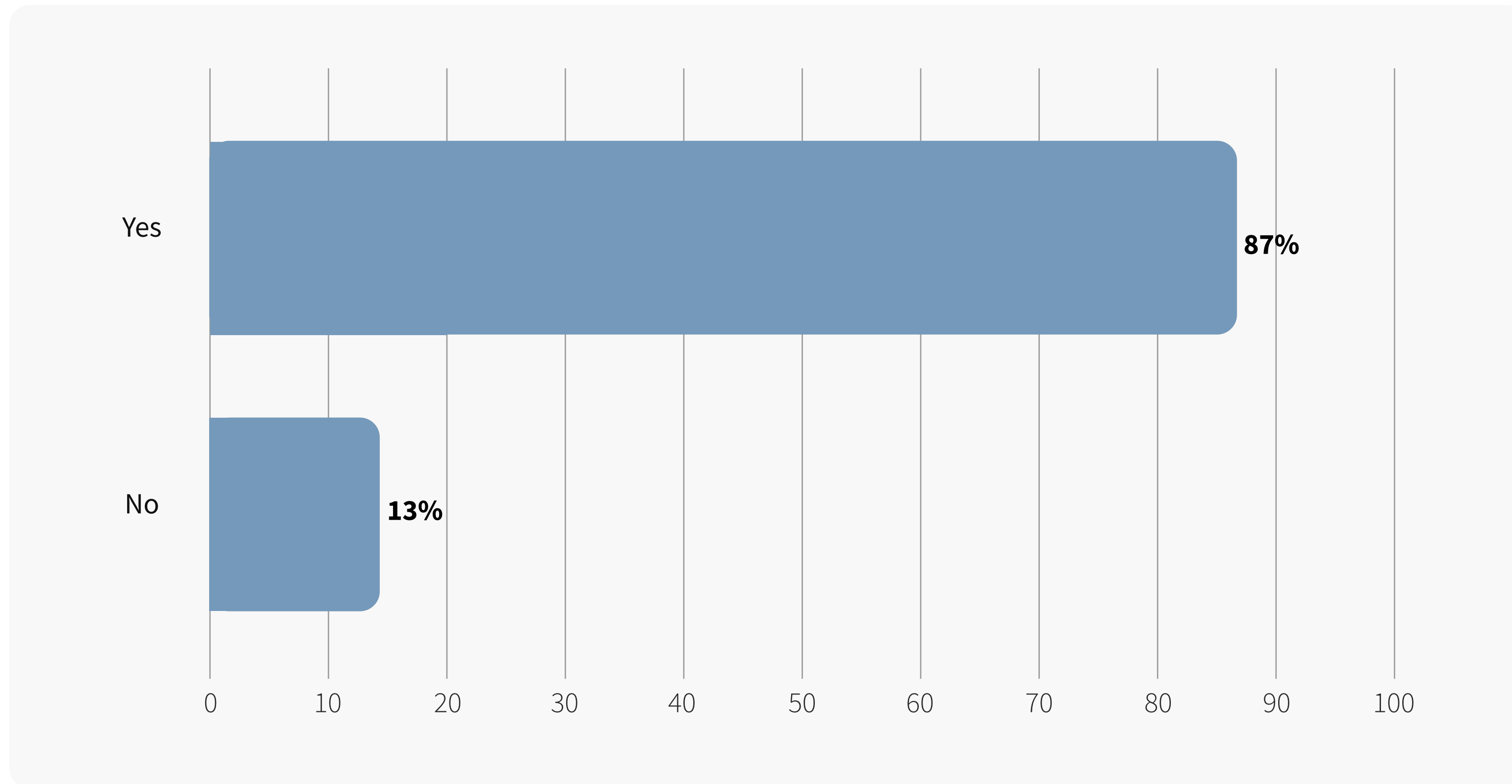Reduction in Systolic
Blood Pressure

50%
Remission or reduction
of Chronic Rash

20%
Reduction in fasting
Blood Glucose levels

Percent of members that would recommend the Digbi Health Program to someone suffering from a chronic disease

80% +
participants were extremely satisfied with the Digbi Health

85% +
participants would recommend the Digbi Health program to another individual suffering with obesity and/or obesity related comorbidities

[This figure is formulated from survey data of participants who would recommend the Digbi Health program].

Conclusion

Obesity is a multifactorial disease arising from an at-risk genetic profile, as well as environmental risk factors such as physical inactivity, insufficient sleep, excessive caloric intake, medications, socioeconomic status, endocrine disruptors, and dysbiosis of the gastrointestinal microbiome. [23] Obesity affects more than 40% of Americans. [23] Even more alarming are the healthcare costs and economic implications associated with obesity and its comorbidities. Insulin-related illness cost $250 billion annually, gastric diseases cost $150 billion annually, cardiovascular hypertension cost $113 billion annually. [10][14][19] These three co-morbidities account for almost 15% of the U.S.' $3.6 trillion annual healthcare costs. [24]

Based on a study using a micro-simulation on the obese population of the U.S., it was determined that for every pound of weight lost it was translated to $62.50 per pound saved in healthcare costs.[25]

1 Pound
Lost

$62.50
Saved

Conclusion

456.6 lbs
LOST
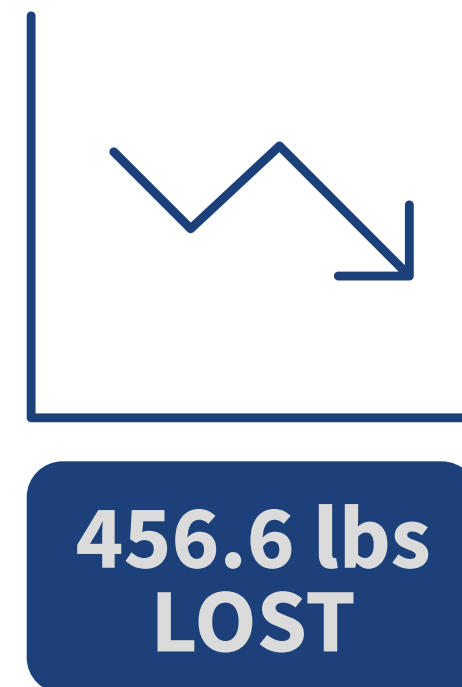
Digbi Health (Mountain View, CA) is an innovative healthcare provider focused on caring for and empowering millions of Americans who are struggling under the yoke of ineffective one-size-fits-all diets, programs and the stigma of "poor self-control" while fighting obesity and associated medical conditions. In our cohort of 45 survey participants, a total of 456.6 lbs were lost within these individuals' first 100 days using Digbi Health - a result that translates to almost $30,000 of annual savings related to healthcare alone.[25]

> **In our cohort of 45 survey participants, a total of 456.6 lbs were lost within these individuals' first 100 days using Digbi Health - a result that translates to almost $30,000 of annual savings related to healthcare alone.[25]**

Greater distribution and availability of genetics and gut biome -based precision weight loss intervention can amount to drastic healthcare savings in the population at large.

To date, the best noninvasive interventions have been in lifestyle and dietary changes. Researchers are still in the process of integrating basic science data with clinical research and learning how to apply the results to patient care, [26] but Digbi Health is already doing that and our patients love the program.

What our members are saying:

"This was my 'missing link!' Learning what MY body needs and how it responds was a revelation! I learned I'm not a failure, I was uninformed!"

"I love the focus on prevention instead of only treating symptoms after disease has set in."

"Digbi is a service I believe should be available to every single person regardless of age, fitness level, diet restrictions, health and wealth status. Every single person can benefit from understanding what their unique body needs nutritionally and actively. Many of the results I got from the program I could have never figured out on my own. Because of Digbi, I now have the tools to live the healthiest life possible. I have never felt more empowered to take my health and fitness to the next level and continue to improve."

"It's the most incredible benefit I've ever received through my Health Care. It's something that offers so much value, and is the first program I've ever used that actually works!"

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