Article

A Health Care Professional Delivered Low Carbohydrate Diet Program Reduces Body Weight, Haemoglobin A1c, Diabetes Medication Use and Cardiovascular Risk Markers—A Single-Arm Intervention Analysis

Grant D. Brinkworth 1,*, Thomas P. Wycherley 2, Pennie J. Taylor 1 and Campbell H. Thompson 3

1 Commonwealth Scientific and Industrial Research Organisation (CSIRO)—Health and Biosecurity, Westmead, NSW 2145, Australia
2 Alliance for Research in Exercise, Nutrition and Activity, University of South Australia, Adelaide, SA 5000, Australia
3 Department of Medicine, University of Adelaide, Adelaide, SA 5000, Australia
* Correspondence: grant.brinkworth@csiro.au; Tel.: +61-8-29490-5665; Fax: +61-8-8303-8899

Abstract: This study examined the effectiveness of a health care professional delivered low-carbohydrate diet program (Diversa Health Program) aiming to improve obesity/type-2-diabetes management for people living in Australia. 511 adults (Age: 57.1 ± 13.7 [SD] yrs) who participated between January 2017–August 2021 for ≥30 days with pre-post data collected for ≥1 key outcome variable (body weight and HbA1c) were included in the analysis. Average participation duration was 218 ± 207 days with 5.4 ± 3.9 reported consultation visits. Body weight reduced from 92.3 ± 23.0 to 86.3 ± 21.1 kg (n = 506, p < 0.001). Weight loss was 0.9 ± 2.8 kg (1.3%), 4.5 ± 4.3 kg (5.7%) and 7.9 ± 7.2 kg (7.5%), respectively, for those with a classification of normal weight (n = 67), overweight (n = 122) and obese (n = 307) at commencement. HbA1c reduced from 6.0 ± 1.2 to 5.6 ± 0.7% (n = 212, p < 0.001). For members with a commencing HbA1c of <5.7% (n = 110), 5.7–6.4% (n = 55), and ≥6.5% (n = 48), HbA1c reduced −0.1 ± 0.2%, −0.3 ± 0.3%, and −1.4 ± 1.3%, respectively. For members with a commencing HbA1c ≥6.5%, 90% experienced a HbA1c reduction and 54% achieved a final HbA1c < 6.5%. With inclusion and exclusion of metformin, respectively, 124 and 82 diabetes medications were prescribed to 63 and 42 members that reduced to 82 and 35 medications prescribed to 51 and 26 members at final visit. A health care professional delivered low-carbohydrate diet program can facilitate weight loss and improve glycaemic control with greatest improvements and clinical relevance in individuals with worse baseline parameters.

Keywords: diet; lifestyle; weight loss; glycaemic control; diabetes

1. Introduction

Worldwide and in Australia, 460 million and 1.2 million people, respectively, are estimated to have type 2 diabetes (T2D) [1]. The World Health Organisation estimates 39% of adults worldwide are overweight and 13% are obese; in Australia, 67% of adults (~12.5 million) are estimated to be either overweight or obese [2]. With rates of T2D, overweight and obesity reaching epidemic levels that continue to grow, public health and economic systems are presented with a major challenge [3,4].

Diet remains the first-line treatment of obesity and T2D. Traditionally, public practice guidelines promoted an energy reduced, high carbohydrate, low fat (HC) diet for obesity and T2D management [5–7]. However, several recently published systematic reviews and meta-analyses of well-controlled studies conducted in adults with T2D have shown that compared to a traditional HC diet, a low carbohydrate, high fat (LC) diet promotes greater weight loss, improvement in blood glucose control and reduction in diabetes medication requirements [8–13]. However, availability of these lifestyle interventions have been largely
limited to patients participating in the research studies and few publicly available LC diet programs, targeting obesity and T2D management, are available and have been evaluated. Health care professionals (HCPs) remain the centre point of effective management of T2D [14]. Previous studies have reported weight loss and improved glycaemic control in individuals with T2D with the use of self-management digital and online delivered LC diet programs [15,16]. However, evaluation of public accessible HCP delivered LC programs that integrate health coaches and medical support are required.

The Diversa Health Care Program is a paid subscription-based health service that delivers a personalised LC plan by HCPs including general practitioners, health educators and allied health professionals who provide education, medical monitoring, and supervised care via telehealth. Additionally, members are provided real-time access and virtual group support. The programs aims to improve weight and T2D management for people living in Australia. The purpose of this study was to assess the effectiveness of the Diversa Health Care Program for the management of body weight and metabolic and diabetes risk factors. Specifically, the primary endpoints to assess effectiveness of the program were changes in body weight and glycosylated haemoglobin (HbA1c) at the participants final recorded program consultation visit. Secondary endpoints assessed included blood pressure, waist circumference and blood lipid levels.

2. Methods

2.1. Study Setting, Participants, and Design

This single-arm, pre-post intervention study design, retrospectively analysed data from individuals aged ≥18 years who joined the Diversa Health Program (a private-for-profit entity previously known as ‘The Low Carb Clinic’; VIC, Australia); and paid for their services covering a period of January 2017–August 2021. Individuals (termed members) were self-referred via word of mouth or advertising or referred by physicians to join the program primarily for the purposes of body weight management, diabetes prevention or management, or to address other metabolic health conditions.

Member data were included in the analysis if the member remained in the program for a minimum duration of 30 days (one month) and had at least 2 consultation visits with a health care professional of the Diversa Health Care team, irrespective of data availability for all reported outcomes. For example, member data for weight were included in the absence of HbA1c data, and vice versa. Baseline data were classified as available data recorded at or within 30 days of the first program consultation. Post-program data were classified as the data available for the member at their most recent consultation, or when they were deemed to have discontinued the program. If a member had a gap between program consultation visits of >395 days (1 year plus 30 days) the member was deemed to have discontinued the program and the longer period of their program data was used for analysis (i.e., the period from initial program consultation to the last consultation before the >395 day gap, or the period from when the participant re-commenced the program (if applicable) to their most recent consultation visit). In the latter scenario, the program recommencement consultation measures were classified as the member’s baseline values.

2.2. Intervention

The Diversa Health Care Program is a HCP delivered program providing remote consultations, unlimited technology-enabled communication support, and a personalised LC diet plan, targeting individuals with or at risk of diabetes living in Australia. The user initially subscribes to a membership plan at a minimum monthly cost of $269, $229 or $209 AUD with a 3-, 6- and 12-month commitment, respectively. At initiation, members complete a consultation with a health coach (either an accredited practicing dietitian, registered nurse, or experienced health educator) to set goals, discuss dietary requirements, support needs and implications of a LC diet lifestyle; and medical practitioner to undergo a medical history assessment, review clinical and biochemical blood test results and medication history and implications with participating in the program. The LC diet eating plan is
delivered using a personalised approach that emphasises eating to satiety with ad libitum intake of dietary protein and fat and limiting dietary carbohydrate intake to <30 g/day to achieve a macronutrient intake profile of approximately 5% carbohydrate, 35% protein and 60% fat (sample daily menu plan presented in Table 1). Throughout the program, participants have access to a variety of voluntary support functions and program features but are required to purchase and prepare their own food. These include:

1. **Medical Monitoring**—Medical review with a Diversa Health General Medical Practitioner at a minimum frequency of every 3 months to review pathology results and make necessary medication adjustments.

2. **One-on-One Coaching Real-Time Support**—Live progress review and consultation with a health coach at least monthly and up to weekly. Ongoing support and advice from a health coach via SMS, WhatsApp, Facebook and Email, as required.

3. **Online member Portal**—Access to an online portal in which participants can access/track pathology results, share notes with a health coach and chat via a Live Chat function, and access education resources personally selected by the health coach.

4. **Community**—Access to a range of health coach-led group webinars, with option to learn, connect and share resources with other members via a moderated Facebook community. Family members are provided access to a family-based webinar to support the members journey.

5. **Resources**—Food guides including information of what to eat, meal planning ideas and shopping advice to tailor the dietary plan to individual dietary requirements and sensitivities. Recipes and information fact sheets personally selected by the members health coach.

### 2.3. Data Collection and Study Outcomes

The Diversa Health program team were responsible for the collection and storage of member data, including registration details and clinical information. At each consultation visit, medication prescription was recorded. Additional information including height, body weight, waist circumference, blood pressure, and biochemical data (blood glucose, insulin, HbA1c, blood lipids and liver function markers [alanine aminotransferase—ALT, aspartate aminotransferase—AST, γ-glutamyltransferase—GTT] were attempted to be collected from the participants who voluntarily provided self-reported information or pathology results initiated by the Diversa Health care team or obtained from health checks conducted by their overseeing general practitioner ‘outside’ of the Diversa Health Care team. Established criteria of overweight and obesity by body mass index (BMI) defined by the World Health Organisation [17] [Underweight: <18.5 kg/m\(^2\); Normal Weight: 18.5–24.9 kg/m\(^2\); Overweight: 25–29.9 kg/m\(^2\); Class 1 Obesity: 30–34.9 kg/m\(^2\); Class 2 Obesity: 35–39.8 kg/m\(^2\); Class 3 Obesity: 40+ kg/m\(^2\)] and diabetes status by HbA1c level defined by the American Diabetes Association [18] [Normoglycemia: <5.7%; Prediabetes: 5.7–6.4%; Diabetes ≥6.5%], were used in the analysis for member categorisation. Achievement of diabetes remission was determined using established criteria (HbA1c of <6.5% for at least three months after stopping glucose-lowering medication) established by an expert consensus report [19].

Deidentified data were provided to the research team. As part of the program joining process, individuals participating in the Diversa Health program provided consent to use their data for research purposes and therefore no consent was obtained directly from each individual to undertake this specific analysis and study. The study was approved by the Commonwealth Scientific and Industrial Research Organization (CSIRO) Human Research Ethics Committee (2022_011_LR).
Table 1. Two-day sample meal plan for the Diversa Health Low Carbohydrate Diet eating plan.

| Mealtime       | Day 1                                                                 | Day 2                                                                 |
|----------------|-----------------------------------------------------------------------|-----------------------------------------------------------------------|
|                | Total Daily Intake Excluding Snacks:                                  | Total Daily Intake Excluding Snacks:                                  |
|                | 24 g Carbohydrate, 161 g Fat, 150 g Protein                           | 17 g Carbohydrate, 232 g Fat, 84 g Protein                            |
| Breakfast      | Bacon, Spinach and Mushroom omelette:                                 | Coconut and Chia Pudding:                                             |
|                | - 3 eggs                                                              | - 100 g coconut cream                                                 |
|                | - 50 g diced bacon                                                    | - 6 blueberries                                                      |
|                | - 50 g sliced mushrooms                                               | - ¼ cup chia seeds                                                   |
|                | - 2 tsp butter                                                       | - 20 g toasted coconut                                               |
|                | - 50 g tasty cheese                                                  |                                                                       |
|                | - ½ cup spinach                                                      |                                                                       |
|                | - Pinch of salt                                                      |                                                                       |
|                | Breakfast                                                             |                                                                       |
| Lunch          | Bacon, Spinach and Mushroom omelette:                                 | Pork with Blue Cheese Sauce:                                         |
|                | - 3 eggs                                                             | - 75 g blue cheese                                                   |
|                | - 50 g diced bacon                                                    | - 100 mL cream                                                       |
|                | - 50 g sliced mushrooms                                               | - 2 pork chops                                                       |
|                | - 2 tsp butter                                                       | - 100 g fresh green beans                                            |
|                | - 50 g tasty cheese                                                  | - 1 tbsp butter                                                     |
|                | - ½ cup spinach                                                      | - Salt and pepper to taste                                           |
|                | - Pinch of salt                                                      |                                                                       |
|                | plus side of lemon infused green beans                                |                                                                       |
|                | - Drizzle olive oil                                                   |                                                                       |
|                | - ¼ cup fresh lemon juice                                            |                                                                       |
|                | - 1 tbsp seeded mustard                                              |                                                                       |
|                | - 200 g green beans                                                  |                                                                       |
|                | - Salt and pepper to taste                                           |                                                                       |
| Dinner         | Creaming baked Atlantic salmon on buttery cauliflower mash:          | Bacon, Lettuce, Tomato (BLT) Creamy Salad:                           |
|                | - 1 fillet of salmon with skin (150–200 g)                           | - 150g chicken breast                                                |
|                | - 2 tsp minced garlic                                                | - ½ rasher middle bacon                                              |
|                | - 2 tsp dried basil                                                 | - 1 egg                                                             |
|                | - 1 tbsp butter                                                     | - ½ large tomato                                                    |
|                | - 1 wedge of fresh lemon                                             | - ½ onion                                                           |
|                | - 250 g fresh cauliflower                                            | - 1 cup mixed salad                                                  |
|                | - 15 mL olive oil                                                    | - 15 g mayonnaise, no added sugar                                   |
|                | Snacks (optional)                                                    | - 2 tsp lemon juice                                                 |
|                | 2 hardboiled eggs                                                   | - Pepper to taste                                                   |
|                | 30 g prosciutto                                                      |                                                                       |

g—grams; tbsp—tablespoon; tsp—teaspoon.

2.4. Statistical Analysis

All statistical analyses were conducted using SPSS statistical software (Version 28.0, Armonk, NY, USA). Descriptive statistics calculated included means and standard deviations of continuous variables and proportions for categorical variables. Paired t-tests were used to compare changes in weight, waist circumference, blood pressure, HbA1c, blood glucose, insulin, lipids, and liver function tests. Statistical significance was set at p < 0.05 (two-tail). Of the 511 members that met the data inclusion criteria, 279 (54.6%) had reported data for at least one of the biochemical outcomes assessed; HbA1c, blood glucose, insulin, lipids, and liver function. Consequently, 45.4% (n = 232) of the members included in the analysis had biochemical data missing that could not be analysed. Given the potential for those with and without biochemical data reported to represent different population groups, data for changes in body weight, waist circumference and blood pressure changes were analysed and separately reported for both the entire member group, as well as for the sub-group who reported biochemical data.
3. Results

3.1. Characteristics

Data were made available for 697 individuals who completed the program sign up process. 511 members met the inclusion criteria and had a program duration of at least 30 days with at least 2 consultation visits. Majority of the members were female (296 female (58%), 145 males (28%), 70 (14%) not reported), with an average age of 57.1 ± 13.7 years (n = 455 reported) and participated in the program for an average duration of 218 ± 207 days and had attended an average 5.4 ± 3.9 HCP consultations.

3.2. Body Weight

503 members had data for body weight at initial consultation and during the program (Table 2). Initial average body weight was 92.3 ± 23.0 kg and average weight loss was 6.0 ± 6.6 kg (6.5% [males: 4.9%; females 6.8%]) over an average duration of 216 days (Table 2, Figure 1). 69.4% (n = 349), 49.3% (n = 248) and 22.5% (n = 113) achieved a weight loss of 3%, 5% and 10%, respectively. From initial consultation to final visit, changes in normal, overweight and obesity classifications were: normal weight (14% to 22%), overweight (25% to 29%), class 1 obesity (27% to 26%), class 2 obesity (18% to 13%) and class 3 obesity (17% to 10%). For members with a starting BMI ≥ 25 kg/m² (classified as overweight or obese; n = 429), overall weight loss was −6.9 ± 6.7 kg (−7.0 ± 6.4%); 75.5% (n = 324) achieved 3% weight loss, 54.3% (n = 233) achieved 5% weight loss and 25.4% (n = 109) achieved 10% weight loss.

Figure 1. Body weight before and at final visit for all members and by baseline weight categorisation of normal weight (BMI: 18.5–24.9 kg/m²), overweight (25–29.9 kg/m²), class 1 obesity (30–34.9 kg/m²), class 2 obesity (35–39.9 kg/m²), class 3 obesity (40+ kg/m²). Values are mean ± standard deviation. * p < 0.001 significantly lower compared to commencement.

For all members who reported data for at least one of the biochemical outcomes (HbA1c, blood glucose, insulin, lipids, and liver function) and body weight at the initial consultation and during the program (n = 277, Table 2), members had an initial average body weight of 90.6 ± 22.1 kg and achieved an average weight loss of 7.2 ± 7.3 kg (8.0%) over an average duration of 256 days. 72.9% (n = 202), 58.8% (n = 163) and 30.0% (n = 83) of members achieved a weight loss of 3%, 5% and 10%, respectively. From initial consultation to final visit, changes in body weight classifications were: normal weight (14% to 26%), overweight (27% to 32%), class 1 obesity (31% to 26%), class 2 obesity (15% to 11%) and class 3 obesity (14% to 6%). For these members with a starting BMI ≥ 25 kg/m², overall weight loss was 8.2 ± 7.3 kg (8.4 ± 7.1%). 79.3% (n = 188), 66.2% (n = 157) and 34.6% (n = 82) achieved a weight loss of 3%, 5% and 10%, respectively.
Table 2. Body weight, waist circumference and blood pressure data at commencement (initial consultation) and post program (final visit) of the Diversa Health program for all members.

| Variable | Initial Consultation—All Participants | Initial Consultation—Participants with Pre/Post Program Data | Final Visit | Change | p Value | Duration from Initial Consultation to Last Recorded Observation—Days |
|----------|---------------------------------------|-------------------------------------------------------------|------------|--------|---------|---------------------------------------------------------------|
|          | N (%), Mean (SD)                       | N (%), Mean (SD)                                            | Mean (SD)  | Mean (SD) | Mean (SD) | Mean (SD) | |
| Initial Consultation | 511                                    |                                                             | 218.1 (207.5) | |
| Age (years)   | 455 57.1 (13.7)                       |                                                             | 57.1 (13.7) | |
| Gender        | -                                      |                                                             | -           | |
| Female        | 296 (57.9)                            |                                                             | 57.9        | |
| Male          | 145 (28.4)                            |                                                             | 28.4        | |
| Not reported  | 70 (13.7)                             |                                                             | 13.7        | |
| Weight (kg)   | 92.2 (23.0)                           | 92.3 (23.0)                                                 | 86.3 (21.1) | -6.0 (6.6) | <0.001 | 216.2 (203.2) |
| BMI (kg/m²)   | 32.8 (7.6)                            | 32.9 (7.6)                                                 | 30.7 (6.9)  | -2.2 (2.4) | <0.001 | 217.6 (203.8) |
| Weight status | 499                                    |                                                             | 496         | |
| Underweight BMI: <18.5 kg/m² | 0 (0) N/A | 0 (0) N/A | 1 (0.2) | - | - | |
| Normal Weight BMI: 18.5–24.9 kg/m² | 69 (13.8) 63.5 (8.4) | 67 (13.5) 63.5 (8.4) | 62.6 (8.2) | -0.9 (2.8) | 0.443 | 252.9 (260.9) |
| Overweight Weight BMI: 25–29.9 kg/m² | 122 (24.4) 77.9 (10.7) | 122 (24.6) 77.9 (10.7) | 73.4 (10.5) | -4.5 (4.3) | 0.010 | 208.6 (185.7) |
| Class 1 Obesity BMI: 30–34.9 kg/m² | 134 (26.9) 91.0 (11.3) | 133 (26.8) 91.0 (11.3) | 85.0 (12.2) | -6.0 (5.5) | <0.001 | 233.7 (211.4) |
| Class 2 Obesity BMI: 35–39.9 kg/m² | 89 (17.8) 105.0 (11.6) | 89 (17.9) 105.0 (11.6) | 96.3 (12.7) | -8.7 (7.0) | <0.001 | 205.9 (191.5) |
| Class 3 Obesity BMI: 40+ kg/m² | 85 (17.0) 125.6 (17.9) | 85 (17.1) 125.6 (17.9) | 115.6 (19.2) | -10.0 (8.9) | <0.001 | 189.6 (175.0) |
| Waist Circumference | 104.2 (17.4) | 104.8 (17.2) | 99.1 (15.9) | -5.7 (6.9) | <0.001 | 210.6 (194.9) |
| Systolic Blood Pressure (mmHg) | 138.2 (20.6) | 139.6 (20.6) | 131.0 (18.7) | -8.6 (18.2) | <0.001 | 225.4 (211.9) |
| Diastolic Blood Pressure (mmHg) | 84.6 (13.1) | 81.2 ± 13.1 | 3.7 ± 12.1 | <0.001 | |

BMI—Body Mass Index.

Members classified as having normoglycemia, pre-diabetes or diabetes by HbA1c level at initial consultation experienced a weight loss of 7.9%, 7.4% and 8.5%, respectively, over an average duration range of 252, 262 to 269 days, respectively.

3.3. HbA1c and Diabetes Status

At program commencement, members who reported HbA1c at the initial consultation and during the program (n = 212) had an average HbA1c of 6.0 ± 1.2%. Based on HbA1c
classification levels, 52% (n = 110) had normoglycemia, 26% (n = 54) had pre-diabetes, and 23% (n = 48) had diabetes. At final visit, average reductions in HbA1c were −0.4% (all members combined [males: −0.5%, females: −0.4%]), −0.1% (normoglycemia), −0.3% (pre-diabetes) and −1.4% (diabetes), Table 3, Figure 2. For members commencing with a HbA1c between ≥5.7–6.4% (pre-diabetes classification), at final visit 78% (42/54), 15% (8/54) and 7% (4/54) had experienced a decrease, increase or no change in HbA1c levels, respectively; and 48% (26/54) had reduced HbA1c level to below 5.7%. For members commencing with a HbA1c ≥ 6.5% (diabetes classification), at final visit 90% (43/48), 9% (4/48), and 1% (1/48) had experienced a decrease, increase or no change in HbA1c levels, respectively; 54% (26/48) had reduced HbA1c level to below 6.5%; and 27% (13/48) achieved diabetes remission. At final visit based on HbA1c classification levels, 66.0% (n = 140) had normoglycemia, 23.1% (n = 49) had pre-diabetes and 10.8% (n = 23) had diabetes.

Table 3. Body weight, waist circumference, blood pressure and metabolic risk markers at commencement (initial consultation) and post program (final visit) of the Diversa Health program for members with reported biochemical data.

| Variable                        | Initial Consultation—All Participants | Initial Consultation—Participants with Pre/Post Program Data | Final Visit | Change | p Value | Duration from Initial Consultation to Last Recorded Observation—Days |
|---------------------------------|---------------------------------------|-------------------------------------------------------------|-------------|--------|---------|---------------------------------------------------------------|
|                                 | N (%)                                 | Mean (SD)                                                  | N (%)       | Mean (SD) | Mean (SD) | Mean (SD)                                                      | Mean (SD) |
| Initial Consultation            | 279                                   |                                                             |             |         |         |                                                               | 258.7 (206.8) |
| Age (years)                     | 274                                   | 59.4 (13.0)                                                |             |         |         |                                                               |            |
| Gender                          |                                       |                                                             |             |         |         |                                                               |            |
| Female                          | 176 (63.1)                            |                                                             |             |         |         |                                                               |            |
| Male                            | 91 (32.6)                             |                                                             |             |         |         |                                                               |            |
| Not reported                    | 12 (4.3)                              |                                                             |             |         |         |                                                               |            |
| Weight (kg)                     | 277                                   | 90.6 (22.1)                                                | 277         | 90.6 (22.1) | 83.4 (19.8) | −7.2 (7.3)                                                   | <0.001     |
| BMI (kg/m²)                     | 274                                   | 32.1 (7.1)                                                | 274         | 32.1 (7.1) | 29.5 (6.3) | −2.6 (2.7)                                                   | <0.001     |
| Weight status classification    | 274                                   |                                                             |             |         |         |                                                               |            |
| Underweight BMI: <18.5 kg/m²    | 0 (0)                                 | N/A                                                        | 0 (0)       | N/A     | N/A     | N/A                                                          | N/A        |
| Overweight BMI: 18.5–24.9 kg/m² | 37 (13.5)                             | 63.7 (9.1)                                                | 37 (13.5)   | 63.7 (9.1) | 62.9 (8.5) | −0.8 (2.6)                                                   | 0.071      |
| Class 1 Obesity BMI: 25–29.9 kg/m² | 74 (27.0)                         | 78.3 (11.6)                                                | 74 (27.0)   | 78.3 (11.6) | 72.7 (11.5) | −5.6 (4.6)                                                   | <0.001     |
| Class 2 Obesity BMI: 30–34.9 kg/m² | 84 (30.7)                         | 91.0 (11.0)                                                | 84 (30.7)   | 91.0 (11.0) | 84.2 (12.0) | −6.8 (6.0)                                                   | <0.001     |
| Class 3 Obesity BMI: 35–39.9 kg/m² | 41 (15.0)                         | 106.4 (12.3)                                               | 41 (15.0)   | 106.4 (12.3) | 94.9 (14.3) | −11.5 (8.0)                                                  | <0.001     |
| Class 4 Obesity BMI: 40+ kg/m²  | 38 (13.9)                             | 124.6 (18.3)                                               | 38 (13.9)   | 124.6 (18.3) | 111.7 (19.5) | −12.9 (9.9)                                                  | <0.001     |
| Weight (kg) by glycaemic control classification | 259 | 259 | | | | | |
| Normoglycemia HbA1c: <5.7%      | 158 (61.0)                            | 91.7 (22.7)                                                | 158 (61.0)  | 91.7 (22.7) | 84.6 (20.2) | −7.2 (7.3)                                                   | <0.001     |
| Pre-diabetes HbA1c: 5.7–6.4 %  | 55 (21.2)                             | 87.9 (21.1)                                                | 55 (21.2)   | 87.9 (21.1) | 81.4 (19.4) | −6.5 (6.0)                                                   | <0.001     |
| Diabetes HbA1c: ≥6.5%           | 46 (17.8)                             | 89.2 ± 22.0                                                | 46 (17.8)   | 89.2 (22.0) | 81.6 (19.4) | −7.6 (7.6)                                                   | <0.001     |
| Weight status classification    | 274                                   |                                                             | 274         |         |         |                                                               |            |
| Underweight BMI: <18.5 kg/m²    | 0 (0)                                 |                                                             | 0 (0)       |         | 1 (0.4) | -                                                             |            |
### Table 3. Cont.

| Variable | Initial Consultation—All Participants | Initial Consultation—Participants with Pre/Post Program Data | Final Visit | Change | p Value | Duration from Initial Consultation to Last Recorded Observation—Days |
|----------|--------------------------------------|-------------------------------------------------------------|-------------|--------|---------|---------------------------------------------------------------------|
| **Normal Weight**<br>BMI: 18.5–24.9 kg/m² | 37 (13.5) - | 37 (13.5) - | 70 (25.5) | - | - | - |
| **Overweight**<br>BMI: 25–29.9 kg/m² | 74 (27.0) - | 74 (27.0) - | 87 (31.8) | - | - | - |
| **Class 1 Obesity**<br>BMI: 30–34.9 kg/m² | 84 (30.7) - | 84 (30.7) - | 70 (25.5) | - | - | - |
| **Class 2 Obesity**<br>BMI: 35–39.9 kg/m² | 41 (15.0) - | 41 (15.0) - | 29 (10.6) | - | - | - |
| **Class 3 Obesity**<br>BMI: 40+ kg/m² | 38 (13.9) - | 38 (13.9) - | 17 (6.2) | - | - | - |
| Waist Circumference | 228 103.9 (16.4) | 220 104.5 (16.1) | 97.7 (14.6) | -6.8 (7.2) | <0.001 | 246.3 (191.9) |
| Systolic Blood Pressure (mmHg) | 186 140.2 (21.5) | 167 141.0 (21.1) | 131.6 (19.3) | -9.3 (19.6) | <0.001 | 234.0 (185.9) |
| Diastolic Blood Pressure (mmHg) | 186 84.7 (13.6) | 167 85.0 (13.8) | 81.0 (13.3) | -4.0 (12.3) | <0.001 | 234.0 (185.9) |
| HbA1c | 261 5.9 (1.2) | 212 6.0 (1.2) | 5.6 (0.7) | 0.4 (0.8) | <0.001 | 254.2 (200.1) |
| HbA1c by glycaemic control classification | 261 | 212 |
| Normoglycemia HbA1c: <5.7% | 158 (60.5) | 5.2 ±0.3 | 110 (51.9) | 5.3 (0.2) | 5.2 (0.3) | -0.1 (0.2) | 0.010 | 252.6 (212.0) |
| Pre-diabetes HbA1c: 5.7–6.4% | 55 (21.1) | 6.0 (0.2) | 54 (25.5) | 6.0 (0.2) | 5.7 (0.3) | -0.3 (0.3) | <0.001 | 242.4 (169.3) |
| Diabetes HbA1c ≥6.5% | 48 (18.4) | 7.9 (1.3) | 48 (22.6) | 7.9 (1.3) | 6.5 (0.9) | -1.4 (1.3) | <0.001 | 271.4 (206.9) |
| Fasting Glucose (mmol/L) | 211 6.3 (3.5) | 186 6.1 (1.9) | 6.1 (1.9) | 5.9 (1.3) | -0.3 (1.3) | 0.009 | 246.0 (202.8) |
| Insulin (mU/L) | 234 12.5 (8.5) | 214 12.6 (8.5) | 10.7 (7.1) | -1.9 (6.8) | <0.001 | 241.0 (191.0) |
| Triglycerides (mmol/L) | 258 1.4 (0.8) | 237 1.4 (0.9) | 1.2 (0.5) | -0.2 (0.7) | <0.001 | 243.5 (192.3) |
| Total Cholesterol (mmol/L) | 255 5.5 (1.5) | 231 5.5 (1.3) | 5.6 (1.8) | 0.2 (1.1) | 0.013 | 240.7 (188.7) |
| HDL-Cholesterol (mmol/L) | 255 1.4 (0.4) | 230 1.4 (0.4) | 1.5 (0.4) | 0.10 (0.22) | <0.001 | 241.2 (188.9) |
| LDL Cholesterol (mmol/L) | 250 3.45 ±1.36 | 226 3.42 ±1.22 | 3.60 ±1.63 | 0.18 ±1.02 | 0.009 | 241.5 ±190.1 |
| Liver Function | 267 28.8 (27.7) | 250 29.1 (28.5) | 22.7 (11.7) | -6.4 (27.1) | <0.001 | 253.9 (205.2) |
| AST (U/L) | 262 24.0 (12.6) | 245 24.0 (12.7) | 20.5 (7.1) | -3.5 (12.6) | <0.001 | 256.8 (206.3) |
| ALT (U/L) | 224 27.0 (23.0) | 201 26.4 (19.0) | 20.9 (12.4) | -5.6 (11.5) | <0.001 | 265.1 (216.3) |

BMI—Body Mass Index, ALT—alanine aminotransferase, AST—aspartate aminotransferase, GTT—γ-glutamyltransferase, HbA1c—glycosylated haemoglobin, HDL—high density lipoprotein, LDL—low density lipoprotein.

### 3.4. Metabolic Risk Factors

At final visit, there were statistically significant reductions in population average waist circumference, blood pressure, blood glucose, insulin, triglycerides and liver function markers, and significant increases in average HDL-cholesterol, total and LDL cholesterol (p < 0.05 for all, Tables 2 and 3).
3.4. Metabolic Risk Factors

At final visit, there were statistically significant reductions in population average waist circumference, blood pressure, blood glucose, insulin, triglycerides and liver function markers, and significant increases in average HDL-cholesterol, total and LDL cholesterol (\( p < 0.05 \) for all, Tables 2 and 3).

3.5. Medication

At baseline, a total number of 63 members were prescribed 124 dosages of diabetes medications (including metformin), and 42 members prescribed 82 medication dosages (excluding metformin) (Table 4). Throughout the program, dosage changes of diabetes medications across the subclasses for prescribed users were reported, including medication eliminations, decreases, increases, commencements, or no changes. The proportion of these changes classified as a diabetes medication dosage elimination or decrease was 47.5% (including metformin) and 62.8% (excluding metformin) (Figure 3). At final visit the total number of members prescribed diabetes medication and total dosages prescribed had reduced to 51 members being prescribed 82 dosages (including metformin) and 26 members being prescribed 35 medication dosages (excluding metformin) (Table 4).

Table 4. Frequency of participants prescribed diabetes medication and diabetes medications prescribed at comment and following program participation.

| Number of Participants, \( n \) | Number of Medications Prescribed, \( n \) |
|---------------------------------|---------------------------------|
|                                | Prescribed Initial Consultation | Prescribed Post Program | Prescribed Initial Consultation | Prescribed Post Program |
| Sulfonylurea                    | 11                              | 4                      | 11                              | 4                      |
| SGLT-2                          | 9                               | 2                      | 9                               | 2                      |
| DDP-4                           | 17                              | 12                     | 17                              | 12                     |
| GLP-1                           | 4                               | 8                      | 4                               | 8                      |
| Metformin                       | 56                              | 47                     | 57                              | 47                     |
| Insulin                         | 17                              | 7                      | 26                              | 9                      |
| Diabetes medication—excluding metformin | 42 | 26 | 67 | 35 |
| All diabetes medication—including metformin | 63 | 51 | 124 | 82 |

Figure 2. Haemoglobin A1c (HbA1c) before and at final visit for all members and for those with a baseline HbA1c of <5.7%, 5.7–6.4% and \( \geq 6.5\% \). Values are mean ± standard deviation. * \( p < 0.05 \), † \( p < 0.001 \) significantly lower compared to commencement.
4. Discussion

This study demonstrates a HCP delivered LC diet program is feasible and effective for achieving clinically relevant weight loss, improvements in blood glucose control and reductions in cardiovascular disease risk factors for individuals who are overweight or obese and/or with elevated blood glucose levels. The changes observed have been associated with reduced risk of obesity comorbidities, diabetes-related complications, cardiovascular disease, and health care costs [20–25]. Marked discontinuation or reductions in the usage of diabetes medications were also observed.

4.1. Weight Loss

An overall, 6.0% mean weight loss in the entire study sample was observed after an average program participation duration of ~7 months. Similarly, an average 8.0% weight loss over an 8.5 month period was achieved in the member sub-group who also provided biochemical data. Sensitivity analysis revealed a −7.0% and −8.4% body weight reduction in the entire study sample and sub-sample, respectively, following exclusion of members who had a normal body weight classification at baseline. This is comparable with other commercial weight loss programs delivered by one-on-one meetings with trained consultants including telehealth and e-mail contacts [26], and greater than that previously reported with commercial online programs [27–29].

A 5% weight loss is considered clinically meaningful to reduce the risk of obesity-related comorbidities and health care costs [20]. Although there is a continuum of clinically meaningful weight loss, which varies among individuals and depends on specific comorbidities and complications. Sustained weight reductions of as little as 2–5% have shown

Figure 3. Frequency of medication dose changes by drug class. Bars represent total number and relative frequency of reported dose changes.

![Figure 3. Frequency of medication dose changes by drug class. Bars represent total number and relative frequency of reported dose changes.](image-url)
significant benefits in cardiovascular risk factors [30], and greater weight loss has been associated with greater improvements in obesity-related comorbidities with a reduction in mortality with weight loss >10% reported [20]. Across the entire member cohort, 50% achieved a weight loss of at least 5% and 23% achieved a weight loss of at least 10%. Correspondingly, there was a systematic downward shift across overweight and obese weight classifications, such that the number of participants across the entire sample classified as obese reduced from 62% at baseline to 49% at final visit, with number of participants classified as normal weight increasing from 14% to 22%. It is well accepted a high BMI increases mortality risk, with the BMI range of 18.5 to <25 kg/m² generally associated with lowest mortality risk, and risk increasing as BMI increases throughout the range of BMIs classified as overweight and obese [31,32].

4.2. Blood Pressure

In response to the weight loss achieved, the substantial reductions in blood pressure (−9/−4 mmHg) observed have been associated with clinically significant reduction in risks of diabetes-relations complications, cardiovascular disease, and mortality [20]. Reboldi et al. [33] reported a 13% reduction in stroke risk for each 5 mmHg reduction in systolic blood pressure and an 11.5% reduction in stroke risk for each 2 mmHg reduction in diastolic blood pressure.

4.3. HbA1c

Across the study sample, an absolute HbA1c reduction of 0.4% occurred after 8 months. More specifically, members with a baseline HbA1c level above the diabetes classification [34], experienced a 1.4% HbA1c reduction that is substantially greater than a previous small study that reported an 0.8% absolute reduction in HbA1c in adults with T2D after 32 weeks participation of an online delivered LC diet intervention [16]. Other studies that have administered LC diet programs to patients with T2D using an in-person model for at least 3 months have reported HbA1c reductions between 0.6–1.6% [35–42]. A 0.3% HbA1c reduction is considered a clinically meaningful to reduce diabetes related long-term complications [22,23]. Moreover, the large 1.4% HbA1c reduction observed in those with a baseline HbA1c above the diabetes classification exceeds the standards set by the FDA for approval of pharmacotherapy diabetes treatment [43].

At final visit, the prevalence members with a HbA1c classified as normoglycemic increased and as diabetes declined. Specifically, ~50% of members initially classified as having pre-diabetes and diabetes HbA1c levels at program commencement had lowered their HbA1c levels to a point where they were no longer within the pre-diabetes and diabetes classification, respectively. This result is comparable with the proportion of individuals with T2D who achieved diabetes reversal after 1 year participation in an intensive, digitally monitored continuous care program, including individualised support with telemedicine, health coaching, and guidance using an individualised LC diet [44]. The Diabetes Prevention Program (DDP) Outcomes study showed that reversion to normoglycemia, even if transient, is associated with reduced risk of diabetes [45]. Moreover, the UK Prospective Diabetes Study demonstrated a legacy effect of a period of good blood glucose control over a 10 year follow up in patients with T2D [46]. This suggests that even if diabetes and poor blood glucose control recurs, reversal of pre-diabetes and diabetes status and improvements in blood glucose control observed in individuals participating in the program can translate to reduced risk of future diabetes and/or vascular events.

A large systematic review showed weight loss in patients with T2D is consistently accompanied by HbA1c reduction in a dose-dependent manner (0.1% HbA1c reduction for every 1 kg weight loss) for overall populations [47]; however HbA1c lowering was greater in populations with poor glycaemic control than in well controlled populations with the same degree of weight loss. Similarly, the present results showed stepwise greater HbA1c reductions in individuals classified as normoglycemic, pre-diabetes and diabetes despite comparable weight loss. Despite this, members with a baseline HbA1c above the
diabetes classification cut-off who still had relatively good average glycaemic control (7.9%), achieved a HbA1c reduction that far exceeded the level that could have been expected for the corresponding level of weight loss.

A separate body of evidence has demonstrated in individuals with T2D that reducing dietary carbohydrate can reduce HbA1c levels independent of weight loss [48]. A systematic review and meta-analysis of 10 RCTs conducted in adults with T2D reported greater HbA1c reductions following a LC diet compared to traditional high carbohydrate diet, and that a greater glucose-lowering effect was related to a lower carbohydrate intake [8]. This suggest the prescription of a LC diet in the Diversa Health program may have contributed to the blood glucose lowering effects observed. Collectively, these findings suggest this program and the use of a LC diet may have the greatest clinical relevance and benefits in those with elevated blood glucose levels, prediabetes and T2D.

4.4. Medication Changes

In addition to the decreases in HbA1c levels, concurrent reductions in medications prescribed for blood glucose-lowering medications were reported. Across all diabetes medication classes (including metformin), 63% of the medication dosage changes were either reductions or cessations across the observed participation period. Notably, of the insulin dosage changes reported, 68% were cessations and 18% were reductions. Due to the treatment costs and risk of side effects, including symptomatic hypoglycaemia and weight gain, often observed with drug related glycaemic control [49,50], the treatment approach utilised in this program may be more advantageous to achieve blood glucose management for improved health outcomes with reduced risk compared to drug treatment. Conduct of a health economic analysis would assist to understand the cost effectiveness of the program examined.

4.5. Blood Lipids

The increase in HDL cholesterol and reduction in triglycerides observed is consistent with previously published systematic reviews of randomised controlled trials examining the effects of LC diets [9–13]. These results suggest that a LC diet is an effective approach to improve lipid abnormalities associated with insulin resistance and the metabolic syndrome, which increases CVD risk in T2D [51]. Previous studies have reported that every 1% increase in HDL cholesterol and 1 mmol/L reduction in triglycerides, may constitute a 3% or 8–21% reduction in heart disease risk, respectively [24,25]. Therefore, the 8% increase in HDL cholesterol and 0.23 mmol/l reduction in triglycerides observed in the participating in this program could translate into a substantial reduction in CVD risk.

Despite the favourable changes in HDL cholesterol and triglycerides levels, average LDL cholesterol levels increased at the final visit of the program. This is similar to some [16,39,52–54], but not all [40,55], previous studies that have reported increases in LDL cholesterol with a LC diet. The health effects of any increase in LDL cholesterol in response to consumption of a LC diet has been extensively discussed previously. It is considered that LDL cholesterol particle size may be a stronger predictor of heart disease risk rather than LDL per se [56]. Separate studies have shown that a LC diet tends to increase the size of LDL cholesterol particles and reduce the number of smaller LDL cholesterol particles [57,58], which is considered to reduce heart disease risk [56,59,60]. This suggests the possibility that the increase in LDL cholesterol observed may promote a cardioprotective effect. Further longer-term studies are required to examine the long-term effects on cardiovascular events.

4.6. Liver Function Markers

The observed reduction in the level of liver function enzymes post program is consistent with several previous studies that have shown that weight loss improves blood markers of liver disease including ALT and AST [61–63]. Previous studies have reported that elevated levels of liver enzymes are positively associated with cardiovascular risk factors, metabolic syndrome and T2D risk [64–66].
4.7. Strengths and Limitations

A strength of the study was the broad inclusion of individuals across varying body weights and blood glucose status categories with limited exclusion criteria for program participation, which promotes broad generalisability of the study results. However, it should be acknowledged the program operates on a user-pay delivery model requiring out of pocket payments by members for consultations with HCPs and health services. This may limit representation of individuals with insufficient resources to pay for program access and lower socio-economic populations, who have a higher risk of pre-diabetes and T2D [67]. Further research is required to understand how this program can be embedded into routine health services to achieve wide-scale adoption. The real-world nature of the intervention is a study strength; however, sporadic data reporting creates difficulties in making direct comparisons between individuals and outcomes measures. This highlights the importance of careful consideration in establishing systemic data collection approaches within public health interventions. The single-arm design with no control group and the lack of dietary intake data is a limitation of the study that precludes the ability to determine the specific components of the program/intervention responsible for the changes observed. The study also lacks follow-up data and adverse events were not systematically recorded making it difficult to determine any side-effects from participating in the health program evaluated. Despite often-cited concerns of side-effects with the use a LC diet [68], a recent systematic review reported no significant or clinically important increase in total or serious adverse events in individuals following a LC diet [13]. The relatively short-duration of the program evaluation also limits the understanding of the long-term sustainability and health effects of the changes in weight, blood glucose control and cardiovascular disease risk makers observed. Further long-term studies are required using a randomised controlled trial design that examine clinical endpoints such as diabetes and cardiovascular events that will provide greater understanding of the therapeutic potential of the program evaluated.

5. Conclusions

The present results indicate that an HCP delivered LC diet program can facilitate clinically relevant weight loss and improved blood glucose control in individuals who are overweight or obese and/or with elevated blood glucose levels. This resulted in an overall reversion across obesity and glycaemic levels for diabetes classifications and reductions in diabetes medication use. Further studies are required to determine the longer-term sustainability and health effects of this program and it could be integrated mainstream medical care to have wider impact in the treatment of obesity and T2D.

Author Contributions: Conceptualization, G.D.B. and T.P.W.; methodology, all authors; formal analysis, G.D.B. and T.P.W.; data curation, T.P.W.; writing—original draft preparation, all authors; writing—review and editing, all authors; project administration, G.D.B. and T.P.W.; funding acquisition, G.D.B. All authors have read and agreed to the published version of the manuscript.

Funding: Diversa Health Pty Ltd. Level 3, 534 Church Street, Cremorne, Victoria 3121, Australia.

Institutional Review Board Statement: The study was approved by the Commonwealth Scientific and Industrial Research Organization (CSIRO) Human Research Ethics Committee (2022_011_LR—17 February 2022).

Informed Consent Statement: Deidentified data were provided to the research team to conduct the analysis for this study. Individuals participating in the Diversa Health program provided consent to use their data for research purposes at the time of joining the health program and therefore no consent was obtained directly from each individual to undertake this specific analysis and study.

Data Availability Statement: Data described in the manuscript will not be made available because approval has not been granted by participants.
Conflicts of Interest: The authors declare that they did not receive any personal compensation from the funding source and that the research was conducted in the absence of any commercial, financial, or personal relationships that could be construed as a potential conflict of interest. The funding source had no role in the design of the study, conduct of the analysis, interpretation, and preparation of the results, nor the decision to submit the manuscript for publication.

References

1. International Diabetes Federation. IDF Diabetes Atlas, 10th ed.; International Diabetes Federation: Brussels, Belgium, 2021.
2. Australian Institute of Health and Welfare. Overweight and Obesity. Australian Government. Available online: https://www.aihw.gov.au/reports/australias-health/overweight-and-obesity (accessed on 26 August 2022).
3. World Health Organization. Global Report on Diabetes; World Health Organization: Geneva, Switzerland, 2016. Available online: https://www.who.int/publications/i/item/9789241565257 (accessed on 29 May 2022).
4. WHO Consultation on Obesity (1999: Geneva, Switzerland) & World Health Organization. Obesity: Preventing and Managing the Global Epidemic: Report of a WHO Consultation. World Health Organization. 2000. Available online: https://apps.who.int/iris/handle/10665/42330 (accessed on 12 September 2022).
5. Rodbard, H.W.; Blonde, L.; Braithwaite, S.S.; Brett, E.M.; Cobin, R.H.; Handelsman, Y.; Hellman, R.; Jellinger, P.S.; Jovanovic, L.G.; Levy, P.; et al. American Association of Clinical Endocrinologists medical guidelines for clinical practice for the management of diabetes mellitus. Endocr. Pract. 2007, 13 (Suppl. S1), 1–68. [PubMed]
6. Colagiuri, S.; Dickinson, S.; Gigris, S.; Colagiuri, R. National Evidence Based Guidelines for Blood Glucose Control in Type 2 Diabetes. Diabetes and the NHMRC. Canberra. 2009. Available online: https://www.diabetesaustralia.com.au/wp-content/uploads/National-Evidence-Based-Guideline-for-Blood-Glucose-Control-in-Type-2-Diabetes.pdf (accessed on 29 May 2022).
7. National Health and Medical Research Council. Australian Dietary Guidelines; National Health and Medical Research Council: Canberra, Australia, 2013.
8. Snorgaard, O.; Poulsen, G.M.; Andersen, H.K.; Astrup, A. Systematic review and meta-analysis of dietary carbohydrate restriction in patients with type 2 diabetes. BMJ Open Diabetes Res. Care 2017, 5, e000354. [CrossRef] [PubMed]
9. Sainsbury, E.; Kizirian, N.V.; Partridge, S.R.; Gill, T.; Colagiuri, S.; Gibson, A.A. Effect of dietary carbohydrate restriction on glycaemic control in adults with diabetes: A systematic review and meta-analysis. Diabetes Res. Clin. Pract. 2018, 139, 239–252. [CrossRef]
10. Huntriss, R.; Campbell, M.; Bedwell, C. The interpretation and effect of a low-carbohydrate diet in the management of type 2 diabetes: A systematic review and meta-analysis of randomised controlled trials. Eur. J. Clin. Nutr. 2018, 72, 311–325. [CrossRef] [PubMed]
11. Meng, Y.; Bai, H.; Wang, S.; Li, Z.; Wang, Q.; Chen, L. Efficacy of low carbohydrate diet for type 2 diabetes mellitus management: A systematic review and meta-analysis of randomized controlled trials. Diabetes Res. Clin. Pract. 2017, 131, 124–131. [CrossRef] [PubMed]
12. Li, S.; Ding, L.; Xiao, X. Comparing the Efficacy and Safety of Low-Carbohydrate Diets with Low-Fat Diets for Type 2 Diabetes Mellitus Patients: A systematic Review and Meta-Analysis of Randomized Clinical Trials. Int. J. Endocrinol. 2021, 2021, 8521756. [CrossRef]
13. Goldenberg, J.Z.; Johnston, B.C. Low and very low carbohydrate diets for diabetes remission. BMJ 2021, 373, n262. [CrossRef]
14. Faruqi, N.; Thomas, L.; Parker, S.; Harris-Roxas, B.; Taggart, J.; Spooner, C.; Wong, V.; Harris, M.F. Primary health care provider-focused interventions for improving outcomes for people with type 2 diabetes: A rapid review. Public Health Res. Pract. 2019, 29, e29121903. [CrossRef] [PubMed]
15. Saslow, L.R.; Summers, C.; Aikens, J.E.; Unwin, D.J. Outcomes of a Digitally Delivered Low-Carbohydrate Type 2 Diabetes Self-Management Program: 1-Year Results of a Single-Arm Longitudinal Study. JMIR Diabetes 2018, 3, e12. [CrossRef]
16. Saslow, L.R.; Mason, A.E.; Kim, S.; Goldman, V.; Ploutz-Snyder, R.; Bayandorians, H.; Daubenmiers, J.; Hecht, E.M.; Moskowitz, J.T. An Online Intervention Comparing a Very Low-Carbohydrate Ketogenic Diet and Lifestyle Recommendations Versus a Plate Method Diet in Overweight Individuals With Type 2 Diabetes: A Randomized Controlled Trial. J. Med. Internet Res. 2017, 19, e36. [CrossRef]
17. WHO Consultation on Obesity (1997: Geneva, Switzerland), World Health Organization. Division of Noncommunicable Diseases & World Health Organization. Programme of Nutrition, Family and Reproductive Health. Obesity: Preventing and managing the global epidemic: Report of a WHO Consultation on Obesity, Geneva, 3–5 June 1997. World Health Organization. 1998. Available online: https://apps.who.int/iris/handle/10665/63854 (accessed on 12 September 2022).
18. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2021. Diabetes Care 2021, 44 (Suppl. S1), S15–S33. [CrossRef] [PubMed]
19. Riddle, M.C.; Cefalu, W.T.; Evans, P.H.; Gerstein, H.C.; Nauck, M.A.; Ob, W.K.; Rothberg, A.E.; le Roux, C.W.; Rubino, F.; Schauer, P.; et al. Consensus Report: Definition and interpretation of remission in type 2 diabetes. Diabetes Care 2021, 44, 2438–2444. [CrossRef] [PubMed]
20. Ryan, D.H.; Yockey, S.R. Weight Loss and Improvement in Comorbidity: Differences at 5%, 10%, 15%, and Over. Curr. Obes. Rep. 2017, 6, 187–194. [CrossRef] [PubMed]
21. Arauz-Pacheco, C.; Parrot, M.A.; Raskin, P.; American Diabetes Association. Treatment of hypertension in adults with diabetes. Diabetes Care 2003, 26 (Suppl. S1), S80–S82. [PubMed]
22. Lind, M.; Oden, A.; Fahlen, M.; Eliasson, B. A systematic review of HbA1c variables used in the study of diabetic complications. Diabetes Metab. Syndr. 2008, 2, 282–293. [CrossRef]
23. Lind, M.; Oden, A.; Fahlen, M.; Eliasson, B. The shape of the metabolic memory of HbA1c: Re-analysing the DCCT with respect to time-dependent effects. Diabetologia 2010, 53, 1093–1098. [CrossRef]
24. Marston, N.A.; Giugliano, R.P.; Im, K.; Silverman, M.G.; O’Donoghue, M.L.; Wiviott, S.D.; Ference, B.A.; Sabatine, M.S. Association Between Triglyceride Lowering and Reduction of Cardiovascular Risk Across Multiple Lipid-Lowering Therapeutic Classes: A Systematic Review and Meta-Regression Analysis of Randomized Controlled Trials. Circulation 2019, 140, 1308–1317. [CrossRef]
25. Boden, W.E. High-density lipoprotein cholesterol as an independent risk factor in cardiovascular disease: Assessing the data from Framingham to the Veterans Affairs High–Density Lipoprotein Intervention Trial. Am. J. Cardiol. 2000, 86, 19–22. [CrossRef]
26. Finley, C.E.; Barlow, C.E.; Greenway, F.L.; Rock, C.L.; Rolls, B.J.; Blair, S.N. Retention rates and weight loss in a commercial weight loss program. Int. J. Obes. 2007, 31, 292–298. [CrossRef]
27. Hwang, K.O.; Ning, J.; Trickey, A.W.; Sciamanna, C.N. Website usage and weight loss in a free commercial online weight loss program: Retrospective cohort study. J. Med. Internet Res. 2013, 15, e11. [CrossRef]
28. Thomas, J.G.; Raynor, H.A.; Bond, D.S.; Luke, A.K.; Cardoso, C.C.; Foster, G.D.; Wing, R.R. Weight loss in Weight Watchers Online with and without an activity tracking device compared to control: A randomized trial. Obesity 2017, 25, 1014–1021. [CrossRef] [PubMed]
29. Postrach, E.; Aspalter, R.; Elbelt, U.; Koller, M.; Longin, R.; Schulzke, J.D.; Valentini, L. Determinants of successful weight loss after using a commercial web-based weight reduction program for six months: Cohort study. J. Med. Internet Res. 2013, 15, e219. [CrossRef] [PubMed]
30. Wing, R.R.; Lang, W.; Wadden, T.A.; Safford, M.; Knowler, W.C.; Bertoni, A.G.; Hill, J.O.; Brancati, F.L.; Peters, A.; Wagenknecht, L.; et al. Benefits of modest weight loss in improving cardiovascular risk factors in overweight and obese individuals with type 2 diabetes. Diabetes Care 2011, 34, 1481–1486. [CrossRef] [PubMed]
31. Aune, D.; Sen, A.; Prasad, M.; Norat, T.; Janszky, I.; Tonstad, S.; Romundstad, P.; Vatten, L.J. BMI and all cause mortality: Systematic review and non-linear dose-response meta-analysis of 230 cohort studies with 3.74 million deaths among 30.3 million participants. BMJ 2016, 353, i2156. [CrossRef]
32. Global BMI Mortality Collaboration; Di Angelantonio, E.; Bhupathiraju, S.; Wormser, D.; Gao, P.; Kaptoge, S.; de Gonzalez, A.B.; Mancia, G.; Verdecchia, P. Effects of intensive blood pressure reduction on myocardial infarction and stroke in diabetes: A meta-analysis in 73,913 patients. J. Hypertens. 2011, 29, 1253–1269. [CrossRef]
33. American Diabetes Association. 2. Classification and Diagnosis of Diabetes: Standards of Medical Care in Diabetes-2019. Diabetes Care 2019, 42 (Suppl. S1), S13–S28. [CrossRef]
34. Goldstein, T.; Kark, J.D.; Berry, E.M.; Adler, B.; Ziv, E.; Raz, I. The effect of a low carbohydrate energy-unrestricted diet on weight loss in obese type 2 diabetes patients—A randomized controlled trial. e-SPEN 2011, 6, e178–e186. [CrossRef]
35. Mayer, S.B.; Jeffreys, A.S.; Olsen, M.K.; McDuffie, J.R.; Feinglos, M.N.; Yancy, W.S., Jr. Two diets with different haemoglobin A1c and antiglycaemic medication effects despite similar weight loss in type 2 diabetes. Diabetes Obes. Metab. 2014, 16, 90–93. [CrossRef]
36. Samaha, F.F.; Iqbal, N.; Shchadi, P.; Chicano, K.L.; Daily, A.A.; McGrory, J.; Williams, T.; Williams, M.; Gracely, E.J.; Stern, L. A low-carbohydrate as compared with a low-fat diet in severe obesity. N. Engl. J. Med. 2003, 348, 2074–2081. [CrossRef]
37. Yancy, W.S., Jr.; Foy, M.; Chalecki, A.M.; Vernon, M.C.; Westman, E.C. A low-carbohydrate, ketogenic diet to treat type 2 diabetes. Nutr. Metab. 2005, 2, 34. [CrossRef] [PubMed]
38. Westman, E.C.; Yancy, W.S., Jr.; Mavropoulos, J.C.; Marquart, M.; McDuffie, J.R. The effect of a low-carbohydrate, ketogenic diet versus a low-glycemic index diet on glycemic control in type 2 diabetes mellitus. Nutr. Metab. 2008, 5, 36. [CrossRef] [PubMed]
39. Tay, J.; Luscombe-Marsh, N.D.; Thompson, C.H.; Noakes, M.; Buckley, J.D.; Wittert, G.A.; Yancy, W.S., Jr.; Brinkworth, G.D. Comparison of low- and high-carbohydrate diets for type 2 diabetes management: A randomized trial. Am. J. Clin. Nutr. 2015, 102, 780–790. [CrossRef] [PubMed]
40. Tay, J.; Thompson, C.H.; Luscombe-Marsh, N.D.; Wycherley, T.P.; Noakes, M.; Buckley, J.D.; Wittert, G.A.; Yancy, W.S., Jr.; Brinkworth, G.D. Effects of an energy-restricted low-carbohydrate, high unsaturated fat/low saturated fat diet versus a high-carbohydrate, low-fat diet in type 2 diabetes: A 2-year randomized clinical trial. Diabetes Obes. Metab. 2018, 20, 858–871. [CrossRef]
41. Yamada, Y.; Uchida, J.; Izumi, H.; Tsukamoto, Y.; Inoue, G.; Watanabe, Y.; Irie, J.; Yamada, S. A non-calorie-restricted low-carbohydrate diet is effective as an alternative therapy for patients with type 2 diabetes. Intern. Med. 2014, 53, 13–19. [CrossRef]
42. Lenters-Westra, E.; Schindhelm, R.K.; Bilo, H.J.; Groenier, K.H.; Slingerland, R.J. Differences in interpretation of haemoglobin A1c values among diabetes care professionals. Neth. J. Med. 2014, 72, 462–466. [CrossRef] [PubMed]
45. Perreault, L.; Pan, Q.; Mather, K.J.; Watson, K.E.; Hamman, R.F.; Kahn, S.E.; Diabetes Prevention Program Research Group. Effect of regression from prediabetes to normal glucose regulation on long-term reduction in diabetes risk: Results from the Diabetes Prevention Program Outcomes Study. *Lancet* 2012, 379, 2243–2251. [CrossRef]

46. Klonoff, D.C. United Kingdom prospective diabetes study follow-up studies establish a legacy effect of therapy for hyperglycemia but not hypertension. *J. Diabetes Sci. Technol.* 2008, 2, 922–924. [CrossRef]

47. Gummesson, A.; Nyman, E.; Knuutsson, M.; Karpefors, M. Effect of weight reduction on glycated haemoglobin in weight loss trials in patients with type 2 diabetes. *Diabetes Obes. Metab.* 2017, 19, 1295–1305. [CrossRef]

48. Gunn, M.C.; Nuttall, F.Q. Effect of a high-protein, low-carbohydrate diet on blood glucose control in people with type 2 diabetes. *Diabetes* 2004, 53, 2375–2382. [CrossRef] [PubMed]

49. Action to Control Cardiovascular Risk in Diabetes Study Group; Gerstein, H.C.; Miller, M.E.; Byington, R.P.; Goff, D.C., Jr; Bigger, J.T.; Buse, J.B.; Cushman, W.C.; Genthuy, S.; Isgaard, S.-B.; et al. Effects of intensive glucose lowering in type 2 diabetes. *N. Engl. J. Med.* 2008, 358, 2545–2559.

50. Henry, R.R.; Gumbiner, B.; Ditzler, T.; Wallace, P.; Lyon, R.; Glauber, H.S. Intensive conventional insulin therapy for type II diabetes. Metabolic effects during a 6-mo outpatient trial. *Diabetes Care* 1993, 16, 21–31. [PubMed]

51. Isomaa, B.O.; Almgren, P.; Tuomi, T.; Forsen, B.; Lahti, K.; Nissen, M.; Taskinen, M.R.; Groop, L. Cardiovascular morbidity and mortality associated with the metabolic syndrome. *Diabetes Care* 2001, 24, 683–689. [CrossRef] [PubMed]

52. Yancy, W.S.; Jr Olsen, M.K.; Guyton, J.R.; Bakst, R.P.; Westman, E.C. A low-carbohydrate, ketogenic diet versus a low-fat diet to treat obesity and hyperlipidemia: A randomized, controlled trial. *Ann. Intern. Med.* 2004, 140, 769–777. [CrossRef]

53. Iqbal, N.; Iqbal, M.; Vetter, M.L.; Moore, R.H.; Chittams, J.L.; Dalton-Bakes, C.V.; Dowd, M.; Williams-Smith, C.; Cardillo, S.; Wadden, T.A. Effects of a Low-intensity Intervention That Prescribed a Low-carbohydrate vs. a Low-fat Diet in Obese, Diabetic Participants. *Obes. (Silver Spring)* 2009, 18, 1733–1738.

54. Dyson, P.A.; Beatty, S.; Matthews, D.R. A low-carbohydrate diet is more effective in reducing body weight than healthy eating in both diabetic and non-diabetic subjects. *Diabet Med.* 2007, 24, 1430–1435.

55. Iqbal, N.; Vetter, M.L.; Moore, R.H.; Chittams, J.L.; Dalton-Bakes, C.V.; Dowd, M.; Williams-Smith, C.; Cardillo, S.; Wadden, T.A. Effects of a Low-intensity Intervention That Prescribed a Low-carbohydrate vs. a Low-fat Diet in Obese, Diabetic Participants. *Diabetes Obes. Metab.* 2011, 13, 313–325. [CrossRef] [PubMed]

56. Sniderman, A.D.; Lamarche, B.; Contois, J.H.; de Graaf, J. Discordance analysis and the Gordian Knot of LDL and non-HDL cholesterol versus apoB. *Curr. Opin. Lipidol.* 2014, 25, 461–467. [CrossRef] [PubMed]

57. Pouwels, S.; Sakran, N.; Graham, Y.; Leal, A.; Pintar, T.; Yang, W.; Kassir, R.; Singhal, R.; Mahawar, K.; Ramnarain, D. Non-alcoholic fatty liver disease (NAFLD): A review of pathophysiology, clinical management and effects of weight loss. *BMC Endocr. Disord.* 2022, 22, 63. [CrossRef]

58. Koutoukidis, D.A.; Koshiaris, C.; Henry, J.A.; Noreik, M.; Morris, E.; Manoharan, I.; Tudor, K.; Bodenham, E.; Dunnigan, A.; Jebb, S.A.; et al. The effect of the magnitude of weight loss on non-alcoholic fatty liver disease: A systematic review and meta-analysis. *Metabolism* 2021, 115, 154555. [CrossRef] [PubMed]

59. Koutoukidis, D.A.; Astbury, N.M.; Tudor, K.E.; Morris, E.; Henry, J.A.; Noreik, M.; Jebb, S.A.; Aveyard, P. Association of Weight Loss Interventions With Changes in Biomarkers of Nonalcoholic Fatty Liver Disease: A Systematic Review and Meta-analysis. *JAMA Intern. Med.* 2019, 119, 1262–1271. [CrossRef]

60. Park, E.O.; Bae, E.J.; Park, B.H.; Chae, S.W. The Associations between Liver Enzymes and Cardiovascular Risk Factors in Adults with Mild Dyslipidemia. *J. Clin. Med.* 2020, 9, 1147. [CrossRef]

61. Shang, H.-S.; Yang, B.-H.; Perng, C.-L.; Tang, S.-H.; Lin, C.-M.; Chang, J.-B. Correlation between Liver Function Tests and Metabolic Syndrome in Hepatitis-free Elderly. *J. Med. Sci.* 2015, 35, 182–189.

62. Lallukka, S.; Yki-Jarvinen, H. Non-alcoholic fatty liver disease and risk of type 2 diabetes. *Best Pract. Res. Clin. Endocrinol. Metab.* 2016, 30, 385–395. [CrossRef]

63. Hill-Briggs, F.; Adler, N.E.; Berkowitz, S.A.; Chin, M.H.; Gary-Webb, T.L.; Navas-Acien, A.; Thornton, P.L.; Haire-Joshu, D. Social Determinants of Health and Diabetes: A Scientific Review. *Diabetes Care* 2020, 44, 258–279. [CrossRef] [PubMed]

64. Freedman, M.; King, J.; Kennedy, E. Popular diets: A scientific review. *Obes. Res.* 2001, 9, 1S–40S. [CrossRef] [PubMed]