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PROTOCOLO – versión *post-print*

Esta es la versión aceptada, revisada por pares. El artículo puede recibir modificaciones de estilo y de formato.

Translational study of obesity management using the Diabetes Prevention Program "Group Lifestyle Balance" in primary care clinics and public hospitals from México: study protocol

Estudio traslacional para el manejo de la obesidad utilizando el Programa de Prevención de Diabetes "Grupo de Equilibrio de Estilo de Vida" en clínicas de primer nivel y hospitales públicos de México: protocolo de estudio

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ABSTRACT

Introduction: Obesity is the main modifiable risk factor for the development of chronic diseases in Mexico. Several randomized controlled trials have shown that intensive lifestyle programs are efficacious for the management of obesity. These programs include frequent sessions (14 or more contacts in the first 6 months) focused on diet and physical activity and use a behavior change protocol. However, most Mexican primary care clinics and public hospitals apply traditional treatments for obesity management with limited results on weight loss. The purpose of the study is to evaluate the effectiveness of the Diabetes Prevention Program (DPP) "Group Lifestyle Balance" for weight loss among adults with overweight and obesity from baseline to 6 months and from baseline to 12 months in primary care clinics and public hospitals from Sonora, México **Material and methods:** This is a translational, multi-center, non-controlled, 6 and 12-month follow-up clinical study with a pre-test and post-test design. Healthcare providers from two primary care clinics, two hospitals and one university clinic will be trained with the DPP protocol to implement on their overweight and obese adult patients. Body weight, body mass index, waist circumference, systolic and diastolic blood pressure, depression, quality of life and stress scales will be measured in participants receiving the program at baseline, 6 and 12 months. Biochemical parameters will be measured at baseline and 12 months. The primary outcome is the change in body weight at 6 and 12 months. **Conclusions:** This study will provide scientific evidence of the effectiveness of the DPP protocol as a model for obesity management in real world clinical practice among the adult Mexican population.

Keywords: Diabetes Prevention Program; Translational Medical Research; Weight Loss; Obesity; Life Style; Health Knowledge, Attitudes, Practice.

RESUMEN

Introducción: La obesidad es el principal factor de riesgo para el desarrollo de enfermedades crónicas en México. Varios ensayos clínicos controlados han mostrado que los programas intensivos de cambio de estilo de vida son eficaces para el manejo de obesidad. Estos programas incluyen sesiones frecuentes (14 o más los primeros 6 meses), centradas en hacer mejoras en la dieta y actividad física utilizando un protocolo de cambio de comportamiento. Sin embargo, la mayoría de clínicas de primer nivel y los hospitales públicos aplican tratamientos tradicionales para el manejo de obesidad que tienen resultados limitados. El propósito del estudio es evaluar la efectividad del Programa de Prevención de Diabetes "Grupo de Equilibrio de Estilo de Vida" sobre la pérdida de peso en adultos con sobrepeso y obesidad del inicio a 6 meses y del inicio a 12 meses del seguimiento en clínicas de primer nivel y hospitales públicos de Sonora, México. **Material y métodos:** Este es un estudio clínico multicéntrico traslacional, no controlado con diseño pre y post-prueba a 6 y 12 meses. Los proveedores de salud de 2 clínicas de primer nivel, 2 hospitales públicos y una clínica universitaria serán entrenados con el protocolo del Programa de Prevención de Diabetes, para implementarlo en sus pacientes adultos con obesidad. Se medirá el peso corporal, índice de masa corporal, circunferencia de cintura, presión sistólica y diastólica, así como escalas de depresión, calidad de vida y estrés, al inicio, 6 y 12 meses. Los parámetros bioquímicos se medirán al inicio y a los 12 meses. La variable de desenlace primaria será el cambio de peso a 6 y 12 meses. **Conclusiones:** Este estudio proveerá evidencia científica de la efectividad del protocolo del Programa de Prevención de Diabetes como un modelo para el manejo de obesidad en adultos mexicanos en condiciones de la práctica clínica del mundo real.

Palabras clave: Programa de Prevención de Diabetes; Investigación en Medicina Traslacional; Pérdida de Peso; Obesidad; Estilo de Vida; Conocimientos, Actitudes y Práctica en Salud.

TRIAL REGISTRATION

Registry

ClinicalTrials.gov: NCT02537704

Data set

See Table 1.

Table 1. Trial registration data.

Data category	**Information**
Primary registry and trial identifying number	ClinicalTrials.gov NCT02537704
Date of registration in primary registry	2 September, 2015
Secondary identifying numbers	ClinicalTrials.gov : DPPMEX-077
Source(s) of monetary or material support	University of Sonora
Primary sponsor	University of Sonora
Secondary sponsor(s)	
Contact for public queries	Dr. Rolando Giovanni Díaz Zavala
Contact for scientific queries	giovanni.diaz@unison.mx
Public title	Translational Study for Obesity Management in Mexican Adults Using the "Group Lifestyle Balance Program" (GLBOMEX)
Scientific title	Translational Study for Overweight and Obesity Management in Adults Using the "Group Lifestyle Balance Program" in Primary Care Clinics and Public Hospitals from Sonora, México
Countries of recruitment	México
Health condition(s) or problem(s) studied	Obesity
Intervention(s)	Experimental: Group Lifestyle Balance Program Participants will be assigned to an adaptation of the "Group Lifestyle Balance Program", a behavioral curriculum implemented in the Diabetes Prevention Program Study. The Group Lifestyle Balance Program will be provided weekly for the first 3.5 months, bi-weekly from 3.5 to 6 months and then monthly until 12 months. Health care providers will be trained for the implementation of the intervention. Additionally, participants will attend at least one monthly visit with a nutritionist (individually). The lifestyle objectives for participants will be as follows:

	To lose 5-10% of initial weight through healthy eating. To do 150 minutes of physical activity each week.
Key inclusion and exclusion criteria	Inclusion Criteria: • Adults (>18 years of age and <65) • Overweight or obese (BMI >25 kg/m2 y <50 kg/m2) • Availability and motivation to attend the intervention program • Patients who would benefit from participating in the program according to the health providers • Signing an informed consent Exclusion Criteria: • Medical conditions affecting body weight significantly • Pregnancy or nursing • Bariatric surgery • Being unable to participate in regular moderate physical activity • Blood pressure >160 mm/Hg • HbA1c >9
Study type	Interventional
Date of first enrolment	September, 2015
Target sample size	250
Recruitment status	(This study was ongoing, but not recruiting participants at the time of the submission of protocol). At this time, the status is completed (16/Nov/2017)
Primary outcome(s)	Change in body weight [Time Frame: Change in body weight from baseline to 6 months and change in body weight from baseline to 12 months]
Key secondary outcomes	• Change in waist circumference [Time Frame: Change in waist circumference from baseline to 6 months and change in waist circumference from baseline to 12 months] • Change in body fat percentage [Time Frame: Change in body fat percentage from baseline to 6 months and change in body fat percentage from baseline to 12 months] • Change in the Beck Depression Inventory score [Time Frame: Change in the Beck Depression Inventory score from baseline to 6 months and change in the Beck Depression Inventory score from baseline to 12 months] • Change in the Short Form-36 Health Survey score [Time Frame: Change in the Short Form-36 Health Survey score from baseline to 6 months and change in the SF-36 Health Survey score from baseline to 12 months] • Change in the Perceived Stress Scale (PSS) -14 score [Time Frame: Change in the Perceived Stress Scale (PSS) -14 score from baseline to 6 months and change in the Perceived Stress

	Scale PSS-14 score from baseline to 12 months] • Change in systolic and diastolic blood pressure [Time Frame: Change in systolic and diastolic blood pressure from baseline to 6 months and change in systolic and diastolic blood pressure from baseline to 12 months] • Change in fasting glucose [Time Frame: Change in fasting glucose from baseline to 12 months] • Change in total cholesterol [Time Frame: Change in total cholesterol from baseline to 12 months] • Change in LDL-cholesterol [Time Frame: Change in LDL-cholesterol from baseline to 12 months] • Change in HDL-cholesterol [Time Frame: Change in HDL-cholesterol from baseline to 12 months] • Change in triglycerides [Time Frame: Change in triglycerides from baseline to 12 months] • Change in fasting insulin [Time Frame: Change in fasting insulin from baseline to 12 months] • Change in HOMA-IR [Time Frame: Change in HOMA-IR from baseline to 12 months] • Change in liver enzymes [AST and ALT] [Time Frame: Change in liver enzymes [AST and ALT] from baseline to 12 months]

PROTOCOL VERSION

Issue date: 10-April-2015 (original)

Protocol amendment number: 01 (20-April-2015)

Primary reason for amendment: changes in Section "Methods" regarding including the blood sampling in the procedures. This change was suggested by the Department of Medicine and Health Sciences Research Bioethical Committee of the University of Sonora.

Authors: *RGDZ, BAG*

Revision chronology

10-April-2015 Original

20-April-2015 Protocol amendment number: 01.

FUNDING

This study will be funded by the University of Sonora, who will provide all the materials for the study, consumables, teaching materials, manuals, biochemical reagents and stationery for patients and health providers. Additionally, CONACYT (*Consejo Nacional de Ciencia y Tecnología*) will fund scholarships for two master degree students.

ROLES AND RESPONSIBILITIES

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Authors' contributions

RGDZ designed and wrote the study protocol, *BIAG* collaborated on designing and writing the study protocol and together with *TJMC* coordinated the implementation. TJMC, MEV, MCCP, RMM, JER and MH collaborated on study design. All authors critically reviewed and approved the final version of the manuscript.

Sponsor

University of Sonora. Blvd. Luis Encinas y Rosales S/N, Hermosillo, Sonora, Mexico. C.P. 83000. Hermosillo, Sonora, México. Sponsor had no role in the design of this study and will not have any role during execution, collection, analysis, and interpretation of data; writing of the report; or decision to submit the results for publication.

Committees

Investigators

Preparation of protocol and revisions

Agreement of final protocol

Coordinating centre: (RGDZ, BIAG, TJMC)

Reviewing progress of study

Reviewing the implementation of the study in the public clinics and hospitals

Organization of training course for health care providers

Provide program manuals and instructional materials

Nutrition Promotion Health Center. (BIAG, TJMC)

Collection of data and body composition measurements.

Clinical Biochemistry Laboratory, Department of Medicine. (*MCCP)*

Serum sample collection and biochemical analysis.

Data management and verification (RGDZ, BIAG, TJMC)

Health care providers: (Social service nutrition interns, doctors, nurses).

Participant recruitment

Implementing the lifestyle program in each public clinic and hospital

Nutritional advice for participants

Monitoring and follow-up of participants

INTRODUCTION

Background and rationale

The worldwide prevalence of obesity has increased in the last decades, including developing countries. According to the latest National Health and Nutrition Survey (ENSANUT 2012) in Mexico, the combined prevalence of overweight and obesity in adults was 71.3% (representing 48.6 million people)[1]. Obesity is one of the major risk factors for type 2 diabetes and cardiovascular disease, the leading causes of death among Mexicans[2]. It is widely known that a reduction of 5% in body weight in patients with obesity leads to better glucose levels, plasmatic lipids, insulin sensitivity, decrease in blood pressure and other benefits[3].

The US Expert Panel on Obesity recently suggested intensive lifestyle programs as the gold standard for obesity management[3]. These programs consist of group and individual weekly visits (≥ 14 sessions in the first 6 months of treatment and then monthly) with a trained healthcare provider to achieve positive changes in diet, physical activity and body weight, using a behavior modification protocol based on a workshop manual[3,4].

Studies such as the Diabetes Prevention Program (DPP) and Action for Health in Diabetes – Look AHEAD – showed, in 2 multicenter clinical trials the possibility of adequate weight management through an intensive lifestyle program, using a behavior modification protocol: "Group Lifestyle Balance®"[5,6]. DPP participants lost on average 6.6% (7 kg) a year after treatment and sustained 80% of the weight loss after 2.8 years[5]. There was a 58% reduction in the incidence of diabetes as well as other benefits compared to the control group[5.] The Look AHEAD study applied the same protocol as the DPP and observed similar results. There was an 8.7% weight loss a year after patients participated in the intensive lifestyle program, 4.7% weight loss four years after, and 4.5% eight years after treatment[6]. Along with weight loss, patients in the intervention group exhibited higher diabetes remission[7], plus improvement in risk factors for cardiovascular disease[8], depression[9], sleep apnea[9], and urinary incontinence[10] when compared to the control group.

Most of the health centers, clinics and hospitals (public and private) in Mexico do not apply evidence-based programs such as the intensive lifestyle program defined above. These types of programs are not considered in policies or guidelines for obesity management in México[11,12]. Programs for obesity management usually consist of diet and physical activity recommendations given at monthly or quarterly visits with a doctor or a nutritionist (and sometimes

psychologists)[13]. When these strategies are tested in randomized controlled trials, results range from a reduction of 1.5 kg to an increase of 1 kg at one-year follow-up[14-16].

Since the general population frequently are not experiencing the benefits of treatments based on efficacy studies, several academic healthcare organizations and government agencies have prioritized translational research[17]. Translational research is defined as applied research that aims to translate available knowledge into clinical and public health practice. Several studies have applied the DPP protocol "Group Lifestyle Balance" in real world conditions. These studies have been implemented by diverse healthcare providers in different real world settings (primary healthcare, specialized units, churches, and other establishments) and have shown variable but acceptable results (−2.7% to −6% body weight reduction and improvement in risk factors)[17]. However, evidence is limited, especially in developing countries such as Mexico.

This research group recently observed, in a randomized controlled trial pilot study, that adult obesity control can be substantially improved in the primary care setting[18]. An adaptation of the DPP protocol was implemented, with 12 weekly group sessions; in addition to weekly visits with a nutritionist and meal replacements. The experimental group was compared against a traditional treatment (diet and physical activity recommendations given monthly by a nutritionist). After three months of treatment, the DPP protocol group had a weight loss of 4.7 kg against an increase of 0.4 kg in the traditional treatment group ($P<0.001$)[18]. Sixty-six percent of participants in the intervention group attained a reduction greater than 5% of initial body weight against 0% of the traditional treatment group. There were also significant decreases in body mass index, waist circumference, hip circumference, and percentage body fat[18].

Explanation for choice of comparators

Given that this study attempted to evaluate the translation (dissemination) of a previously validated program into a real world clinical setting (instead of proving efficacy), the study did not include a control group. Additionally, numerous studies have not observed important changes in the body weight of control group participants[5,8,19], including one study implemented in México by our group that shows an increase in body weight[18]. Recently, Johns and colleagues evaluated the weight change of participants randomized to minimal intervention control groups in weight loss trials. The analysis included twenty-nine studies representing 5,963 individuals. They found that the weight loss at 12 months was minimal (-0.8 kg [95%CI: -1.1 to -0.4])[20]. Thus, considering the focus of the study and the evidence mentioned above, we considered a control group to be unnecessary.

Study objectives

Primary Objective

To evaluate the effectiveness of the Diabetes Prevention Program "Group Lifestyle Balance" for weight loss among adults with overweight and obesity from baseline to 6 months and from baseline to 12 months in primary care clinics and public hospitals from Sonora, Mexico

Secondary objectives

The key secondary objectives are to evaluate the effectiveness of the Diabetes Prevention Program "Group Lifestyle Balance" among adults with overweight and obesity for:

- Change in waist circumference from baseline to 6 months and from baseline to 12 months.
- Change in body fat percentage from baseline to 6 months and from baseline to 12 months.
- Change in the Beck Depression Inventory from baseline to 6 months and from baseline to 12 months.
- Change in the Short Form-36 Health Survey score from baseline to 6 months and from baseline to 12 months.
- Change in the Perceived Stress Scale (PSS) -14 from baseline to 6 months and from baseline to 12 months.
- Change in systolic and diastolic blood from baseline to 6 months and from baseline to 12 months.
- Change in fasting glucose from baseline to 12 months.
- Change in total cholesterol from baseline to 12 months.
- Change in LDL-cholesterol from baseline to 12 months.
- Change in HDL-cholesterol from baseline to 12 months.
- Change in triglycerides from baseline to 12 months.
- Change in fasting insulin from baseline to 12 months.
- Change in HOMA-IR from baseline to 12 months.
- Change in liver enzymes [AST and ALT] from baseline to 12 months.

Trial design

This is a translational, multi-center, non-controlled, 6 and 12-month follow-up clinical study with a pre-test and post-test design.

MATERIAL AND METHODS

Study setting

Two public primary healthcare clinics will be included: Dr. Domingo Olivares Health Center and Advanced Primary Healthcare Center; two public hospitals: General Hospital of the State of Sonora and Dr. Ignacio Chávez Hospital; and a public university clinic in Hermosillo, Sonora: Nutrition Health Promotion Center at University of Sonora. Hermosillo is an urban city with 884,273 inhabitants, located in the state of Sonora, northwest of Mexico. The effectiveness of the program in the different levels of healthcare will be evaluated. Relevant authorities from the state government Department of Health (heads of education, social service coordinators, heads of health centers, and officials responsible for obesity management in hospitals) will be invited to participate.

Eligibility criteria

All participants must accept and sign an informed consent form to participate in the study.

Inclusion Criteria

Healthcare providers will recruit patients following the inclusion criteria: adults (aged 18 to 65), with overweight or obesity (BMI: >25 kg/m^2 to <50 kg/m^2), who are motivated and available to attend the intervention program. Only patients who attend at least one individual consultation and a group session will be included. Contrary to efficacy trials, all patients considered to have the potential to benefit from the program through weight loss, healthy diet, and moderate physical activity will be included, even if they suffer from certain health conditions (hypothalamic obesity, hypothyroidism, Cushing syndrome, under medical treatment) or are taking medication (biguanides, sulfonylureas, etc.) affecting weight. People who are unable to read will be able to participate if they have a literate support person who can come along with them to the sessions.

Exclusion Criteria

Pregnant women or women who breastfed in the last 6 months, bariatric surgery, glycated hemoglobin $\geq$ 9%, patients taking insulin, systolic blood pressure $\geq$160 mm/Hg, or patients who are negatively affected by weight loss or physical activity will be excluded.

Eligibility criteria for study centers and individuals who will perform the interventions

The study will be divided into two phases. In the first phase healthcare providers will be trained, and in the second phase program implementation and evaluation at 6 and 12 months will take place.

The first phase will focus on training and standardization of healthcare providers (nutritionists, social service nutrition interns, and physicians) of participating clinics to implement the intervention program. Institutions interested in participating will need a designated area for patient consultation (including basic anthropometric equipment) and a classroom for group sessions. An essential requirement for the institutions will be to have a nutrition intern for nutritional counseling of the participants. In Mexico it is mandatory for nutrition students that at the end of their four-year academic formation, they conduct 1 year of social service in public health institutions without financial remuneration. This group represents a potential population of competent health providers at low cost for the dissemination of the program in the health sector in Mexico.

Healthcare provider training

The training course will last for 35 hours and include two modules. The first module will focus on clinical evaluation of the patient with obesity, covering topics like dietary management, etiology, diagnosis and treatment[21], and will include study of recent scientific literature on updates and successful interventions, and the US guidelines for obesity management[3-4,22,23]. The second module will be dedicated to training the healthcare providers on an adaptation of the Diabetes Prevention Program protocol "Group Lifestyle Balance®" http://www.diabetesprevention.pitt.edu/index.php/for-the-public/group-lifestyle-balance-materials/. The adapted manual is made up of 32 topics, divided into 25 sessions; with nutrition aspects, physical activity, and behavior strategies. Additionally, topics on standardization of anthropometric measurements will be included (Table 2).

Table 2. Healthcare Provider Training.

Hours	Topics
5	▪ Introduction to overweight and obesity management in adults with the "Lifestyle Balance" program in public clinics and hospitals in Sonora ▪ Format utilization ▪ Standardization of anthropometric measurements
5	▪ Intensive lifestyle modification programs for obesity management. Why are these the gold standards in obesity management? (Results from the Diabetes Prevention Program (DPP); The Look AHEAD study; a Mexican translational study using the DPP; and US Guidelines (2014) for adult obesity management) ▪ How to evaluate and treat the obese patient
25	**Adaptation of the DPP protocol "Group Lifestyle Balance Program"®** Session 1. "Welcome to the Lifestyle Balance Program®" Session 2. "Fat and calorie detective" Session 2.1 "Reading a nutrition label" Session 2.2 "Cooking demonstration" and "Food weighing"* Session 3. "Move those muscles" Session 4. "Food groups" and "Portion sizes"* Session 5. "Healthy eating" and "Calorie balance tilting" Session 6. "Take control of what is around you" Session 7. "How to design your own menu (Mexican System for Food Equivalents)"* Session 8. "Problem solving" Session 9. "Four key points to eating out healthily" and "The slippery path to lifestyle change" Session 10. "Make social signs work in your favor" and "Activity plan kickoff" Session 11. "You can manage your stress" Session 12. "How to feel motivated" Session 13. "Obesity risks"* Session 14. "Diabetes prevention"* Session 15.1 "Heart health and cholesterol"*

	Session 15.2 "Heart health and hypertension"*
	Session 16. "Relationship between obesity and cancer" *
	Session 17. "Getting ready for long-term self-control" and "Adjust your thoughts for long-term self-control"
	Session 18. "More volume, less calories" and "Conscious eating"
	Session 19. "Strengthen your exercise program"
	Session 20. "Stretching: the truth about flexibility"
	Session 21. "Rise for your health"
	Session 22. "Looking at the past and looking at the future"

* Additional session to the original program.

The providers will be handed a file with color-printed materials: Patient manual (Spanish version) and Provider manual (Spanish version, adapted by our research group) to work with during the program. Formats to register measurements of the study variables (weight, height, waist circumference, and blood pressure), formats for follow-up, attendance lists for patients, a chronogram of activities and additional material will also be supplied.

Healthcare providers must attend every single training course session. The research group will have frequent contact with the participating healthcare providers. The training team will consist of three health professionals: one of them with a PhD in Science (GD-Z) and two Nutritional Sciences graduates with experience using the DPP protocol (BA-G and TM-C).

Interventions

Interventions

The Intensive Lifestyle Intervention Program

The intervention program will last for a year, the first three and half months will be intensive; patients will attend weekly group sessions (14 sessions), and at least one individual session but up to four individual sessions per month (depending on the healthcare provider and patient agreement and within the available time and space at the clinic). During months 3.5 to 6 the intervention will be less intensive with one group session every 2 weeks (5 sessions) and one individual session every month. After 6 months, group sessions and individual sessions will be scheduled once a month. The goal for each participant will be to lose 10% of initial body weight.

Behavior change protocol (group sessions). Each participant will be handed an adaptation of the DPP protocol "Group Lifestyle Balance" manual, which includes topics such as weight loss and healthy lifestyle benefits, learning healthy eating, physical activity and active lifestyle benefits, calorie intake and balance, stimulus control training, problem solving strategies, assertive thinking and communication, control of negative thoughts, relapse and solutions, stress management, self-control techniques, self-motivation, positive reinforcement, etc. (Table 2).

The original "Group Lifestyle Balance" Patient manual and the Provider manual were adapted (original versions available for free on http://www.diabetesprevention.pitt.edu/index.php/for-the-public/group-lifestyle-balance-materials/ We added topics on: "Cooking demonstration" and "Food weighing", "Food groups" and "Portion sizes", "How to design your own menu (Mexican

System for Food Equivalents)", "Obesity risks", "Diabetes prevention", "Heart health and cholesterol", "Heart health and hypertension" and "Relationship between obesity and cancer". Cultural adjustments were also made to the content to fit the Mexican context. For example, we used the Mexican System for Food Equivalents for nutrition prescriptions because nutrition interns are familiar with its use and it includes typical food for Mexico. Likewise, most dynamics employed in the group sessions were developed by the research group.

Participants will gradually aim for 150 minutes (2.5 hours) per week of physical activity, as well as a reduction in fat intake (33-55 g, depending on the participant's baseline weight).

Individualized nutrition session. The first weekly session with the healthcare provider will last between 40 to 60 minutes; subsequent sessions will be 20 to 30 minutes long. A medical history that includes dietary evaluation, anthropometry, biochemistry results and physical activity will be completed for each participant. Total energy expenditure (TEE) will be estimated and their diet restricted by 500 to 1000 kcal.

Calorie intake will range from 1200-1800 kcal/day (depending on each participant's TEE); macronutrient distribution as follows: 55% carbohydrate, 20% protein, and 25% lipids[24]. Meal replacements will be recommended as a substitute for 2 meals each day (breakfast and dinner); these will be used to improve weight loss[25]. In Mexico, the midday meal is the main meal of the day. Whole meal plans will be given to participants for the second month. During the third month, patients will be taught to create their own meal plan using a food exchange system[26].

Patients will be able to buy commercial meal replacements (a product used in previous studies will be recommended[8]) or make a milkshake at home (milk, fruit, nuts, and 5 g of psyllium fiber). Patients will also be given the option of choosing a meal plan elaborated by a nutritionist if they do not want to take meal replacements.

Modifications

Participants who become pregnant during the intervention period, initiate other weight control treatment, or withdraw their informed consent will be excluded from the study.

Adherence

During each individual session, weight, goal progress, adherence to the meal plan, and adverse signs and symptoms will be checked and questions answered. Daily food intake and physical activity (minutes) recording will be recommended for each patient. If the participant is not able to

attend a group or individual session, a call will be made to schedule the next appointment. A roll call will be made in all group sessions. Telephone calls will be made by the coordinating center when patients do not attend more than two sessions or follow-up consultations.

Concomitant care

Patients will not be prohibited from any treatment that benefits their health; however those that can have a significant effect on body weight will be recorded.

Outcomes

The primary outcome will be the mean change in body weight from baseline to 6 months, and from baseline to 12 months.

Secondary outcomes will include mean changes in other obesity parameters (waist circumference, body fat percentage), systolic and diastolic blood pressure, mental health measurements (depression, health-related quality of life, and perceived stress) from baseline to 6 months and from baseline to 12 months, in addition to changes in biochemical parameters (fasting glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, fasting insulin, HOMA-IR, AST and ALT) from baseline to 12 months.

Participant timeline

See Figure 1.

Figure 1. Schedule and duration of study time periods.

	STUDY PERIOD														
	Screening	**Initial Assessment**	**Treatment (months 1-6)**						**Middle Assessment**	**Treatment (months 7-12)**					**Final Assessment**
MONTH	*-1*	**0**	*1*	*2*	*3*	*4*	*5*	*6*	*6*	*7*	*8*	*9*	*10*	*11*	*12*	*12*
ENROLMENT:																
Recruitment	X															
Eligibility screen	X															
Informed consent	X															
INTERVENTIONS:																
[Group Lifestyle Balance Program]		X	♦	—	—	—	—	♦	X	♦	—	—	—	—	♦	X
ASSESSMENTS: [*Medical History and Demographic*]		X														
[*Concomitant Medication*]		X							X							X
[Body weight]		X							X							X
[Waist circumference		X							X							X
[Body fat percentage]		X							X							X
[Beck Depression Inventory score]		X							X							X

[Short Form-36 Health Survey score]		X							X								X
[Perceived Stress Scale (PSS) -14 score]		X							X								X
[Systolic and diastolic blood pressure]		X															X
[Fasting glucose]		X															X
[LDL-cholesterol]		X															X
[HDL-cholesterol]		X															X
[Triglycerides]		X															X
[Fasting insulin]		X															X
[HOMA-IR]		X															X
[Liver enzymes (AST and ALT)]		X															X

Sample size

Group sample sizes were determined based on the main objective of this study, which is to determine changes in body weight from baseline to follow-up using a paired mean test. For that reason, group sample sizes were obtained through a paired t-test formula, considering data from a previous one year study with a mean weight loss of 4.2 kg and a standard deviation of 5.6[27]. In this way, using a two-tailed paired t-test, a significance level of 0.05 and power of 0.8, a sample size of 14 participants for each center[28] was obtained. However, to allow for dropouts and the translational focus of the study, 50 subjects per center will be recruited (5 centers in total). This increase guarantees that group samples sizes will be also adequate for other exploratory comparisons.

Recruitment

Posters, flyers, Facebook page, direct invitation from nutritionists or social service nutrition interns, doctor and nurse referrals will be used to invite participants into the study. Meetings will take place to inform interested patients. Once patients are recruited in each clinic, they will be divided into groups of 25 to 50 people for the group sessions.

Data collection methods

Study measurements will take place during months 0, 6 and 12 in the Nutrition Health Promotion Center at the University of Sonora.

Primary outcome

Weight will be collected using standard techniques[29]; with a SECA MBCA (Medical Body Composition Analyzer, SECA Gmbh & Co. Kg Hammer Steindamm 9-25).

Anthropometric and Body Composition measurements

Height will be measured using a SECA stadiometer, model 284 (Seca Gmbh & Co. Hammer Steindamm 9-25, Germany; capacity 30-220 cm) with the participant in the Frankfort Plane, without shoes and facing forward[25]. Waist circumference will be measured at umbilical level[29] with a fiberglass

anthropometric tape (GÜLICK, 0 to 150 cm). Fat percentage will be estimated by SECA MBCA (Medical Body Composition Analyzer, SECA Gmbh & Co. Kg Hammer Steindamm 9-25). A digital sphygmomanometer (Omrom, model HEM-907XL) will be used to measure systolic and diastolic blood pressure in duplicate[30].

Biochemical parameters

A comprehensive assessment and evaluation of the effect of weight loss on biochemical parameters will be measured following standardized techniques: fasting glucose, total cholesterol, LDL-cholesterol, HDL-cholesterol, triglycerides, aspartate aminotransferase (AST), alanine-aminotransferase (ALT). Fasting insulin will be used as a marker for insulin resistance (HOMA-IR)[31]. Venous blood sampling and analysis will be performed at the Clinical Biochemistry Laboratory of Medicine at the University of Sonora.

Mental health measurements

To evaluate psychological variables, the participants will answer three questionnaires. The questionnaires will be administered by staff with the support of a psychologist with expertise in the area. The Beck Depression Inventory will be used to assess the effect of the program on depression[32] and health-related quality of life (HRQOL) will be evaluated with the SF-36 health survey[33]. To measure the effect of the program on stress, the Perceived Stress Scale, PSS-14[34] will be applied.

Retention

Phone calls will be made when patients miss more than two consecutive sessions. No economic incentive will be given to patients for attending the 6 and 12 month measurements. In order to have the largest amount of data from the participants for the analysis, those who decide to leave the intervention will still be asked to attend the 6 and 12 month measurements with the purpose of obtaining the primary variable of the study (to allow and intention-to-treat analysis).

Participant Withdrawal

Participants may withdraw from the study at any time they wish. Participants will be withdrawn from the study if they become pregnant within the period of the study or if they start an alternative treatment for weight loss.

Data management

In order to have quality data, double verification will be carried out by the study staff. The plausibility of the data will also be checked and any outlier will be carefully reviewed.

Cost of the program

Participating patients will not pay for the program (patient manual and materials for educational sessions) or individualized nutrition sessions in any of the centers but will be responsible for buying the meal replacements (if they choose them) and any food consumed at home. Health providers will not pay any cost for the training, materials, etc.

Statistical methods

Data will be presented as mean and standard deviation (mean ± SD) for normally distributed variables, and medians and percentiles (25-75) will be used for variables with a non-normal distribution. A paired t test (or Wilcoxon rank-sum test in the case of a non-normal distribution) will be used to evaluate the change from baseline to follow-up in the primary outcome (weight) and secondary variables (BMI, blood pressure, etc.) for each center. The primary and secondary outcomes at 6 and 12 months will be analyzed using completers and also by intention-to-treat analysis. We will make an effort to obtain the outcome measurements at 6 and 12 months for all participants who dropped out of the study to include these data in the intention-to-treat analysis. For subjects not participating in the 6 and 12 month measurements the baseline value will be used (baseline value carried forward) for the intention-to-treat analysis. We will perform some exploratory subgroup analysis to assess the effect of sex, age group, income, attendance at visits, diabetes status, obesity category, use of medications affecting weight, on the primary outcome. We will also evaluate if there are differences (at 6 and 12 months from baseline) between centers using one way ANOVA or Kruskal-Wallis test (with Bonferroni or Dunn´s post hoc analyses) for normal or non-normal distributed continuous variables and chi-square (χ^2) analyses for categorical variables with Bonferroni post hoc test. A p value $\leq$ 0.05 from a two-tailed test will be used as a criterion for statistical significance (p

value ≤ 0.05). Statistical software NCSS 10 will be utilized to analyze data (Number Cruncher Statistical System for Windows, Kaysville, UT, USA).

Data monitoring

This study does not have an external data monitoring committee. The progress of the study will be presented every six months to the group of researchers participating in the study. Also, once the final evaluations of the study are concluded, the results will be presented to the Department of Medicine and Health Sciences Research Bioethical Committee of the University of Sonora and to the Medical Center "Dr. Ignacio Chavez" Research Committee at ISSSTESON). No interim analysis is programmed for this study.

Harms

This section was not considered in the protocol, but this kind of intervention is considered as very low risk.

DISCUSSION

To our knowledge this trial will be the first to present scientific evidence on the implementation of a translational study in a developing country. This study will open up opportunities to improve clinical practice in México and other developing countries.

Some studies where the DPP protocol is implemented in real life conditions have had positive results (6.9 kg in a year)[35], similar to those observed in efficacy studies (approximately 7 kg in a year)[5]. Nonetheless, there have been interventions with less favorable results (0.45 kg to 3.3 kg in weight loss)[36,37]; making it crucial to have a protocol which is specific to the country's culture and healthcare system.

The study's strengths include its translational approach. An evaluation connected to real world conditions will take place, including possible problems attached to clinical practice in public settings, such as high patient flow, lack of space, infrastructure and personnel, high activity demand, resistance to change, help of students in training (nutrition interns), etc. Several public clinics are included and the study sample was estimated to detect changes in body weight in each clinic, making it possible to evaluate the effect of the program at different levels of healthcare. Healthcare providers participating will be nutrition interns with no previous experience in obesity management; meaning optimal generalization of results.

ETHICS AND DISSEMINATION

Research ethics approval

The present protocol was approved by the Department of Medicine and Health Sciences Research Bioethical Committee of the University of Sonora (2015-Apr-10) and by the Medical Center "Dr. Ignacio Chavez" Research Committee at ISSSTESON (CEI-015-2015).

Health care professionals from the medical centers and clinics, patients and other relevant groups will be informed about the results of this trial. Additionally, the findings of this study will be presented at relevant academic congresses and published in peer-reviewed journals.

Consent or assent

Participants will receive information about the study by health providers in the clinics. Additionally, the research staff will ensure the understanding of the study and ask the participants to sign a consent form.

Confidentiality

All the participants' information will be protected under identification codes and stored in both physical and electronical forms. Study investigators will have full access to the data.

Declaration of interests

No potential conflict of interest was reported by the authors. Rolando Giovanni Díaz-Zavala declares no conflicts of interest; Brianda Ioanna Armenta-Guirado declares no conflicts of interest; Teresita de Jesús Martínez-Contreras declares no conflicts of interest; Maria del Carmen Candia-Plata declares no conflicts of interest; Julián Esparza-Romero declares no conflicts of interest; Raúl Martínez-Mir declares no conflicts of interest; Michelle Haby declares no conflicts of interest; Mauro E. Valencia declares no conflicts of interest.

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