RESEARCH PROTOCOL

The effect of individual and mixed incentives on diabetes management: Part 2

Sponsor:

Medical Research Council (MRC), United Kingdom

Version 1.0

April 2016

TABLE OF CONTENTS

RESEARCH TEAM

NATIONAL TEAM:

Jaime Miranda, MD, PhD

Principal Investigator
Research Professor, UPCH School of Medicine
Email: Jaime.miranda@upch.pe

Antonio Bernabé-Ortiz, MD, MPH

Researcher on Chronic Diseases
Universidad Peruana Cayetano Heredia
Email: Antonio.Bernabe@upch.pe

Francisco Diez Canseco, BA, MPH

Research Associate at CRONICAS
Email: fdiezcanseco@upch.pe

M. Amalia Pesantes, MA, MPH, PhD

Postdoctoral Fellow
Email: maria.pesantes.v@upch.pe

INTERNATIONAL TEAM:

Antonio J. Trujillo, PhD

Co-PI

Director, Master of Health Science in Health Economics, Department of International Health
Associate Professor, Johns Hopkins School of Public Health
Email: atrujil1@jhu.edu

Katherine Sacksteder, PhD

Associate, Johns Hopkins School of Public Health
Email: ksacksteder@yahoo.com

CONTACT DETAILS

For further information, please do not hesitate to contact:

(1) Dr. Jaime Miranda

E-mail jaime.miranda@upch.pe, or call +511-241-6978.

(2) Dr. M. Amalia Pesantes

E-mail maria.pesantes.v@upch.pe, or call +511-241-6978.

RESEARCH SITES

Name of the research site	**:**	Hospital Nacional Arzobispo Loayza
Address	**:**	Avenida Alfonso Ugarte 848
Principal Investigator	**:**	Dr. Socorro del Pilar Cornejo
Telephone	**:**	6144646, Extension 4300

PROTOCOL SUMMARY

This research study aims to compare the impact of a financial incentive on improving glycated hemoglobin control in patients with type 2 diabetes mellitus, depending on whether the effort is made individually or with someone's support (family member, friend).

The use of financial incentives to promote behavioral changes that persist over time has been tested in other countries in the region. They have been used to change habits such as smoking, and to lose weight; however, there are no studies that allow to know the impact of this strategy in managing type 2 diabetes mellitus. There are also no clear strategies for determining the amount of financial incentive to be used to promote behavioral changes (adherence to treatment, increasing physical activity, and a healthy diet) in patients with type 2 diabetes mellitus. There are also questions regarding the frequency of the incentives, the type of incentive (cash or other type of reward), the payment method, etc.

This research study is exploratory in nature, as it is oriented to document the implementation process of an intervention focused on reducing weight and glycated hemoglobin in patients with type 2 diabetes mellitus who will receive a financial incentive in three modalities: (1) individual (only the patient receives the incentive), (2) predetermined mixed (the patient and the person who assists him/her in achieving his/her goal receive the incentive and divide it according to what is established by the research protocol), and (3) negotiated mixed (the patient and the person who assists him/her in achieving his/her goal receive the incentive and divide it after negotiating between them the percentage corresponding to each one). The financial incentive will be accompanied with diabetes education.

At the end of the pilot study, qualitative research methods will be used to document the experiences and opinions of research participants on the relevance of the use of financial incentives to promote habits associated with the management of diabetes mellitus.

1. INTRODUCTION

Diabetes is a chronic disease presenting an enormous challenge to healthcare systems worldwide. Diabetes management recommendations such as lifestyle changes, increased exercise, and dietary modifications have proven to be an effective way to reduce the long-term consequences and costs of disease. Even though we know that these practices are effective, adherence is poor among patients with diabetes. For example, in Peru, 70% of patients with diabetes have poor glycemic control and only 3.3% meet the optimal control definition according to the recommendations of the American Diabetes Association (ADA), i.e., adequate control of glycemia, LDL cholesterol and blood pressure. [1] In the general population, the values obtained for glycemic control are equally poor. Only 7% of the population has an adequate glycemic control and treatment (measuring fasting blood glucose) and if the criteria are stricter (glycated hemoglobin or HbA1c <7%), then only 0% of the population has adequate disease control. [2] Poor management of a chronic disease such as diabetes is associated with a high risk of chronic complications and comorbidities, raising costs associated with healthcare.

1.1. Diabetes prevention

Clinical trials in developed countries and population-based studies have reported preventive care benefits for glycated hemoglobin control in patients with diabetes. [3] Preventive strategies focused on diabetes management can add up to four years of life expectancy to a 50-year-old person, reduce diabetes-related morbidity, and significantly increase well-being.[4] Despite the medical consensus on the efficacy of preventive measures, patient medication adherence worldwide is quite poor. A research study carried out in seven Latin American cities on subjects with type 2 diabetes showed that 78% of the individuals were aware of their condition, 33% were receiving treatment, and only 5% met therapeutic goals.[5] A research study carried out in Lima showed similar results: 71% were aware of their disease, 40% were receiving treatment and only 7% met therapeutic goals.[2]

Low levels of adherence can be caused by behavioral factors of patients with diabetes, preventing them from doing what is best for their health. Factors such as failure to control or poor planning capacity for the future could contribute to this low level of prevention; in addition to traditional factors such as access to healthcare services and lack of economic resources to pay for prevention. In this context, the use of pure and mixed financial incentives could help with the problems patients face in doing what is in their best interest to take care of their health.

1.2. Incentives in Healthcare

Factors preventing the person with diabetes from seeing the benefits of taking care of him/herself could change if a reward is offered to the person with diabetes that gives him/her a present benefit and helps him/her deal with everyday efforts to take care of him/herself. The literature on incentives suggests that the effect of incentives to modify behavior depends on several interconnected factors.[6] The payment of monetary incentives based on compliance with certain prevention measures reduces the cost of disease management; however, it may end up displacing the internal individual motivation that is key to the self-care of a patient with a chronic disease. Both the design and mode of delivery of incentives can affect the success of the intervention.

The existing literature does not allow us to state if monetary incentives promote lasting behavioral change and there are many doubts about their relevance for chronic disease management.[7] Monetary rewards can help with short-term habit formation as the benefits of prevention accrue over longer periods of time. Prevention today can lead to reduced prevention efforts tomorrow, and monetary incentives can help to consolidate this initial process.[8] However, cash rewards may not be high enough to drive initial changes, especially once the initial effort effects dissipate. It can also be argued that monetary incentives can be effective in rewarding concrete results, but less effective in rewarding processes such as checking blood sugar levels every day or exercising.

Behavioral science literature states that incentives given to individuals should be: frequent and in small amounts, be positive rather than negative, and promote the connection between short- and long-term goals.[9-11] Evidence on the impact of financial incentives is growing as there are several interventions that seek to demonstrate the benefits of using financial incentives for

adherence to substance abuse treatment,[12] and to promote weight loss and smoking cessation.[13,14] More recently, studies regarding the effects of incentives on blood donation, organ donation, HIV treatment, and other pro-social behaviors have been carried out.[15,16-17]

On the other hand, there are behaviors in which it is not easy to measure the effort made by the patient to reach them. Financial incentives may not be effective as in the case of weight loss, since two people may lose the same amount of weight in the same amount of time, but the effort to reach the goal probably differed. Some reviews indicate that financial incentives are effective in the very short term for preventive care and in well-defined behavioral interventions; furthermore, there is enough evidence to affirm that financial incentives are effective for the long-term lifestyle change required for health promotion. [18]

Little is known about the effect of incentives at an individual level when such incentives are given to peers, a family member or friend who provides support in this process. These incentives are called "mixed incentives" and can also positively influence individual behavior, as they use the feeling of connection with others and responsibility to support each other.

1.3. Diabetes and Financial Incentives

There have been very few research studies evaluating the effectiveness of financial incentives in patients with diabetes and the impacts of this disease. A randomized clinical trial with a small sample size conducted in the United States used financial incentives in African American veterans with poor glycemic control and found that the incentive slightly improved HbA1c results by 1 to 2% over 6 months; however, the result was not statistically significant.[20] Other research studies have demonstrated the role of financial incentives in stimulating and maintaining weight loss in people who wanted to lose weight. While one research study found that lottery-style incentives could facilitate weight loss compared to a control group, the effect was not maintained after the incentive was removed.[21] However, in another research study in which incentives were linked to group success, group-incentive participants not only lost more weight, but also maintained weight loss better than the control group.[21] These results are interesting, and suggest further research study is needed on incentives in diabetes management.

1.4. Do financial incentives work in Latin America?

Conditional cash transfers (CCTs) have become a widely used method by governments as a strategy to try to reduce poverty, improve education, and other major aspects of development (such as child nutrition), particularly in Latin American countries.[8] Several Latin American countries have some CCT programs, such as Mexico, Honduras, Nicaragua, Brazil, Colombia and Peru. Recent evaluations of the impact of these programs show that health indicators are improving as an outcome of them. [22] It is important to clarify that most of the outcomes come from process indicators and are directly related to the use of healthcare services.

The first CCT program implemented in Latin America was "Oportunidades" in Mexico, requiring children and pregnant women to take nutritional supplements and attend certain healthcare services. An evaluation of the program found an association between a greater number of transfers received and significantly better outcomes in many areas, including short- and long-term memory, visual integration, and language development.[23]

"Atención a Crisis", a CCT in Nicaragua, is conditional on the fact that families receiving the money must ensure that preschoolers attend their medical appointments on a regular basis and get vaccination and micronutrients/food supplements when necessary. The evaluation of this program found significant improvements in healthcare outcomes. Interestingly, these improvements continued even two years after the program and cash transfers ceased.[24] *"Juntos"*, the CCT in Peru was designed as a poverty reduction initiative through increasing the demand for public services in exchange for fulfilling certain responsibilities related to health and education, and pregnant women and mothers of children aged below 5 are required to use certain healthcare services. Families benefiting from "Juntos" receive a cash transfer of 200 Nuevos Soles every two months. *"Juntos"* is a relatively new program and there are not many published research studies describing its impact. A World Bank report found that overall household consumption increased by 33% and poverty levels were reduced by 14%.[24] In addition, it found that *"Juntos"* increased the likelihood that children in beneficiary households would comply with their growth and development check-ups (CRED, by its Spanish acronym), seek professional help in case of any illness, and the likelihood that pregnant women would give birth in a health facility attended by an expert professional.

To better understand the impact of cash component of CCT, it is important to recognize that these programs take advantage of strong family structures in Latin America, and leverage the responsibility of their members for health improvement. The person in charge of ensuring that the

requirements are met is not only encouraged to be responsible because of an individual reward, but to improve the family's situation. This underscores the potential of using social capital and accountability to design more effective policies, and will be an important element of our approach. As has been demonstrated in CCT programs, the use of financial incentives has the potential to reach long-term effects that last beyond the duration of the incentive program, leading to greater public health impact.

Recent research analyzes factors explaining disease self-management in people with diabetes and hypertension using cross-sectional databases for five Latin American countries.[25] The findings suggest that income level is the most important component in reducing differences in the impact of preventive practices. In the five countries of the study, the role of income in the diabetes self-management of diabetic patients ranged from 23% in Chile to 58% in Argentina. It is interesting to note that access to healthcare services (insurance availability) [26] and knowledge about diabetes self-management have a significantly lower impact than income. All these outcomes suggest that cash payment may play an important role in changing an individual's behavior in the case of patients with diabetes.

1.5. Justification

Clinical trials in developed countries and population-based studies indicate that there are many benefits of preventive care in patients with diabetes.[3, 27] Despite the medical consensus on the effectiveness of preventive measures, worldwide it is difficult to reach control targets in patients with diabetes. The available data clearly emphasize the need for a research study on what methods are needed for diabetes prevention today, and why it is needed specifically in Latin America and other resource-poor settings.

Globally, very few studies have been conducted to evaluate the effectiveness of incentives in diabetes. In this application, we aim to explore the role of incentives in changing the behavior of people with type 2 diabetes. Cost savings or cost-effective interventions can avoid the economic impact of long-term complications of diabetes, such as retinopathy, nephropathy, neuropathy and cardiovascular diseases, as well as short-term complications, such as hospitalizations due to poor glycemic control.[28]

In our research study we will apply financial incentives to promote behavioral change in our patients in order to improve their glycemic control.

2. RESEARCH OBJECTIVES

The outcomes of this research study will be used to design a randomized clinical trial aimed at evaluating the impact of the use of monetary incentives in patients with type 2 diabetes mellitus. For this purpose, we first have to answer two research questions, as specified below.

General Objective:

To compare the implementation processes of three interventions that use financial incentives to promote behavioral changes in patients with type 2 diabetes mellitus in order to identify barriers and facilitators linked to the implementation process of each intervention.

Specific Objectives

- To document patient experience in the study of financial incentives.
- To document the experience of people accompanying patients with type 2 diabetes mellitus.
- To test the acceptability and clarity of instructional material used to promote behavioral change.
- To test the feasibility of reaching the proposed clinical goals (weight loss and glycated hemoglobin).
- To test the "sufficiency" of the incentive amount given to both the patient and the patient's companion, in order to promote behavioral changes.
- To explore the sustainability of the companion's participation for 9 months.
- To explore activities that could make the companion more effective in helping the patient manage his/her diabetes.
- To explore whether the patient is able to keep a daily record of the effort made in managing his/her diabetes.
- To evaluate the feasibility of packaging and implementing a future clinical trial, which will evaluate the impact of the use of monetary incentives in patients with type 2 diabetes mellitus.

3. RESEARCH METHODOLOGY

3.1. Research design

Pilot study testing the feasibility of implementing three types of intervention with financial incentives in a randomized fashion.

3.2. Research site

Endocrinology Outpatient Services of the Hospital Nacional Arzobispo Loayza.

3.3. Study population, selection criteria

The study population in general will be patients with type 2 diabetes mellitus who meet the inclusion criteria and people in their social environment who consent to participate in the role of companions throughout the intervention.

3.3.1 Inclusion criteria for the patient

Subjects will be eligible if

1. They have a diagnosis of type 2 diabetes mellitus,
2. They aged 18 to 70 years,
3. They receive treatment with Metformin or their treatment consists of dietary changes.
4. They have a body mass index between 25kg/m2 to 39.9 kg/m2 (range that includes from overweight to severe obesity),
5. They are able to consent,
6. They are not fulfilling the role of a companion in the framework of this pilot study.
7. They do not have blindness, amputations or foot ulcers nor are receiving dialysis as a consequence of diabetes mismanagement.

3.3.2 Inclusion criteria for the companion

The companions will be chosen by the patients and must also:

1. Aged 18 to 70 years,
2. Not have any physical or mental condition that would prevent them from fulfilling the role in assisting the participant to lose weight,
3. Have availability of time and commitment to support the participant in achieving his/her weight loss goals.
4. Be able to consent.

Consent to participate in the research study will be signed after confirming all inclusion criteria have been met.

3.3.3 Exclusion criteria

- Subjects will be excluded from enrollment if they have cancer or another severe comorbidity.
- Subjects will be excluded if they report pharmacological treatment for weight loss or corticosteroids.
- Subjects will be excluded if they are pregnant.

3.4. Sample size

Seventy-five people (patients and companions):

- 45 patients assigned to three intervention groups, 15 in each group (see section 3.5).
- 30 companions: Since two of the groups will require a companion, 30 people will be enrolled to be with the participant throughout the intervention.

3.5. Intervention

Before starting the intervention, the diabetes educator (DE) will explain the research study to the patients and answer their questions. Informed consent will be obtained from each participant and their companion prior to enrollment in the study. Baseline information will be taken, including demographic data, socioeconomic status, time of illness, treatment, chronic complications of diabetes and comorbidities, anthropometric measurements (weight, height, blood pressure), and laboratory measurements (baseline glycated hemoglobin): (Annex 1).

Previously, the DE will contribute to the preparation of materials on nutrition and physical activity for people with diabetes and will have a flipchart for use in the training sessions (Annex 2).

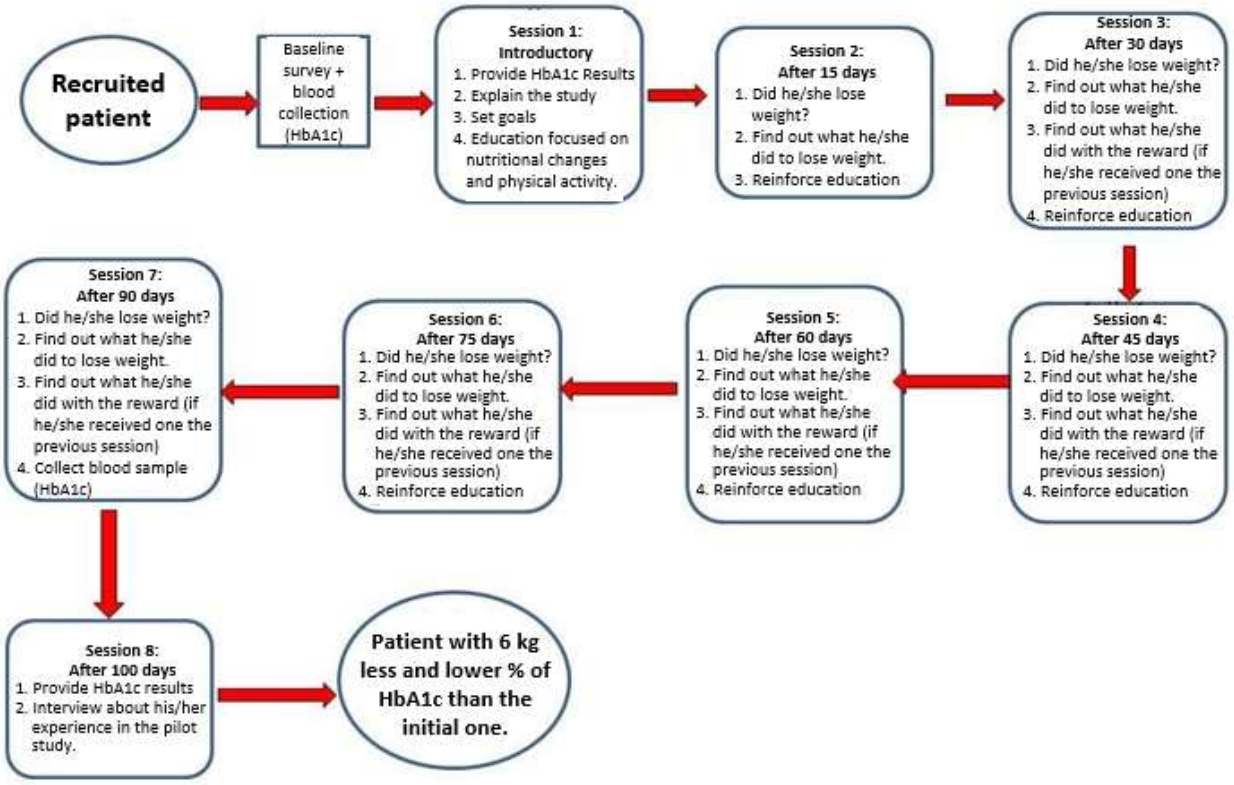
Patients will be randomized to one of the three interventions to be evaluated:

Intervention 1: Individual Incentives.

1. Participants will receive information about the study, specifying that they will receive a reward of 150 soles (about 25% of the minimum wage) at each meeting if they have managed to lose one kilogram in a two-week period. The meetings will take place every two weeks for three months.
2. An initial assessment will be made to determine their weight and the results of their Hba1c will be provided.
3. A plan will be made to determine how many kilograms they should have at each biweekly meeting (Annex 3).
4. Education on nutrition and physical activity will be provided.

5. A manual with information on nutrition and physical activity for people with diabetes interested in losing weight will be given, including tips for loosing weight and a weight loss plan for a two-week period (Annex 4). The DE will manage an "ideal" weight loss plan for the patient throughout the 3 months of the study.
6. They will be given a diary to enter their daily diet and physical activity. The information in this diary will be the starting point to discuss with the diabetes educator at each session about the barriers and achievements in the implementation of the weight loss plan (Annex 4).
7. In addition to the introductory meeting, they will attend seven follow-up sessions (See Figure 1) and a final one in which he/she will be rewarded with the same amount (150 soles) if he/she managed to lower their HbA1c by at least 1%.

Figure 1: Patient route map



Intervention 2. Mixed incentives: *Set up by researchers*

1. Participants and their companions will receive information about the study, specifying that they will receive a reward of 150 soles (about 25% of the minimum wage) at each meeting if they have managed to lose one kilogram in a two-week period. The meetings will take place every two weeks for three months. The reward will be divided 50% for the participant and 50% for the companion.
2. An initial assessment will be made to determine the patient's weight and the results of his/her Hba1c will be provided.
3. A plan will be made to determine how many kilograms they should have at each biweekly meeting (Annex 3).
4. Education on nutrition and physical activity will be provided orally and/or with the support of audiovisual material.
5. A tri-fold leaflet will be given to the companion to guide his/her support (Annex 5).
6. A manual with information on nutrition and physical activity for people with diabetes interested in losing weight will be given to the patient, as well as tips and the weight loss plan per fortnight. The diabetes educator will manage an "ideal" weight loss plan for the patient throughout the 3 months of the study (Annex 4).
7. They will be given a diary to enter their diet, which will be the starting point to discuss with the diabetes educator at each session about the barriers and achievements in the implementation of the weight loss plan (Annex 4).
8. In addition to the introductory meeting, they will attend seven follow-up sessions and a final one in which he/she will be rewarded with the same amount (150 soles) if he/she managed to lower their HbA1c by at least 1%.

Intervention 3. Mixed incentives: Set up by participants

1. Participants and their companions will receive information about the study, specifying that they will receive a reward of 150 soles (about 25% of the minimum wage) at each meeting if they have managed to lose one kilogram in a two-week period and if the companion supports the process by attending all the biweekly follow-up meetings. The meetings will take place every two weeks for three months. The participant and the companion must negotiate on the day of the meeting in which the reward is given how they will distribute the amount received, specifying that the maximum that one party can receive is 80% and the minimum 20% of the total amount.
2. An initial assessment will be made to determine the patient's weight and the results of his/her Hba1c will be provided.
3. A plan will be made to determine how many kilograms they should have at each biweekly meeting (Annex 3).
4. Education on nutrition and physical activity will be provided orally and/or with the support of audiovisual material.

5. A tri-fold leaflet will be given to the companion to guide his/her support (Annex 5).
6. A manual with information on nutrition and physical activity for people with diabetes interested in losing weight will be given to the patient, including tips for loosing weight and a weight loss plan for a two-week period. The diabetes educator will manage an "ideal" weight loss plan for the patient throughout the 3 months of the study (Annex 4).
7. They will be given a diary to enter their diet, which will be the starting point to discuss with the diabetes educator at each session about the barriers and achievements in the implementation of the weight loss plan (Annex 4).
8. In addition to the introductory meeting, they will attend seven follow-up sessions and a final one in which he/she will be rewarded with the same amount (150 soles) if he/she managed to lower their HbA1c by at least 1%.

3.5 Outcomes

At the end of the three months, a comparison will be made between the achievements in terms of (1) weight loss and (2) glycated hemoglobin to then assess through qualitative research whether the amount of money given was the right one to promote weight loss, the role of education in diabetes and the process assessment.

3.6 Recruitment process

3.6.1 Randomization and other processes

The recommendations of the CONSORT statement [26] will be followed in the randomization process. An investigator who is independent of the research process and is not involved in its activities will be responsible for randomization. For this purpose, a randomization in blocks of 4 will be used using pre-coded sealed envelopes to conceal the allocation. This process will be carried out one week after signing the consent form and the initial assessment.

3.6.2 Procedures

Screening

All patients attending the endocrinology outpatient service of the Hospital Arzobispo Loayza will be invited to participate in an initial assessment to determine if they are eligible to participate in the study. This assessment consists of: (1) verifying if the participant is overweight, obese or severely obese (but not morbidly obese), (2) confirming that they have someone in their close social circle (family or friends) who are of legal age and healthy and would be willing to fulfill the role of "companion" which consists of supporting them throughout the pilot study in order to reach their weight loss goals, (3) confirming that their diabetes treatment consists of Metformin or dietary changes. Those patients who meet the inclusion criteria will be invited to participate in the study and once they accept, a blood sample will be collected to document their baseline HbA1c levels.

Phase 1: Baseline

Baseline information will be collected including demographic data, socioeconomic status, relevant background information such as time since diagnosis, type of antidiabetic drugs, lifestyle (smoking, alcohol consumption and physical activity), depression, presence of diabetes complications and comorbidities (See Annex 1). Anthropometric measurements such as weight, height and blood pressure, and blood tests such as glycated hemoglobin (HbA1c) will also be included.

Phase 2: Intervention

The patient will be contacted within three days of signing the consent form and their participation will be confirmed. Then the participants will be randomized. Those participants in intervention group 1 should not bring their companion to any of the meetings while in the case of intervention 2 and 3, the companions should sign a commitment to support the patient during the weight loss plan and to share the reward.

Subsequently, all selected patients will fill out the "Personality Inventory" survey to collect data on non-cognitive skills. (See Annex 6).

Phase 3: Weight loss follow-up

The follow-up will be carried out by a professional person qualified as a Diabetes Educator who will be trained by the project staff to follow up the 45 patients and their companions.

Arm1: Individual Incentives

Participants will be required to come every 2 weeks to measure their weight and to collect a blood sample for glucose measurement with a glucometer. Weight will be measured in fasting conditions, using the same scale and at the same time as the previous visit.

Each participant will attend a total of 8 sessions (including the initial meeting). In sessions 2 to 7 the diabetes educator will weigh them to see if they reached the goal.

- ***If they reached the goal***: They will be rewarded and asked about the actions taken to reach their goal. In addition, suggestions for improving their nutrition and diabetes management will be reviewed. For this purpose, the information entered by the participants in their diary will be used. They will also be asked about their physical activity, adherence to treatment and changes in their eating habits. If they have received a reward in the previous session, they will be asked about how they used that reward.

- ***If they did not reach the goal:*** They will be asked about the actions they took to lose weight and the main challenges in implementing them. For this purpose, the information entered by the participants in their diary will be used. Suggestions for improving their nutrition and diabetes management will be reviewed. They will also be asked about their physical activity, adherence to treatment and changes in their eating habits.
- The patient will fill out a diabetes self-management questionnaire at each session (See Annex 4).

In session 7, a blood sample will be collected to measure his/her Hba1c. The results will be given in session 8 (last session) in which he/she will be rewarded if his/her Hba1c has dropped at least 1% since the beginning of the study (See Annex 7).

Arm 2: Mixed Incentives: Set up by Researchers

Participants will be asked to come for a weight measurement every 2 weeks and for the collection of a blood sample to measure glucose with a glucometer, if possible, together with their companions. Each pair (patient and companion) will attend a total of 8 sessions. The reward is conditional on the presence of the companion. In sessions 2 to 7 they will be weighed by the diabetes educator.

- ***If they reached the goal***: The patient and the companion (if present) will be rewarded. If the companion is not at the meeting, the nurse will contact him/her by phone to coordinate the date and time when he/she can come to receive his/her part of the reward. The patient and the companion will be asked about the actions taken to reach their goal. In addition, suggestions for improving nutrition and diabetes management will be reviewed. For this purpose, the information entered by the participants in their diary will be used and a short questionnaire oriented to self-report adherence, physical activity and dietary changes will be administered. In case of having received a reward in the previous session, they will be asked about how they used it.
- ***If they did not reach the goal:*** They will be asked about the actions taken to lose weight and the main challenges to implement them. For this purpose, the information entered by the participants in their diary will be used. Suggestions for improving nutrition and diabetes management will be reviewed. In addition, a short questionnaire oriented to self-report adherence will be administered. In session 7, a blood sample will be collected to measure his/her Hba1c. The results will be given in session 8 (last session) in which he/she will be rewarded if his/her Hba1c has dropped at least 1% since the beginning of the study, and if

his/her companion has been with him/her.

Arm 3: Mixed Incentives: Set up by Participants

Participants will be required to visit every 2 weeks, if possible with their companions, to measure their weight and to collect a blood sample for glucose measurement using a glucometer. Each pair (patient and companion) will attend a total of 8 sessions. In sessions 2 to 7 the diabetes educator will weigh them.

- ***If they reach the goal***: The patient and the companion should negotiate, based on the effort perceived by each of the parties, what percentage of the reward corresponds to each one, with the condition that the maximum percentage to be received is 80% and the minimum is 20%. The patient and the companion (if present) will be rewarded. If the companion is not at the meeting, the negotiation will take place by telephone and then the nurse will call him/her to coordinate the date and time when he/she can come to receive his/her part of the reward. The patient and the companion will be asked about the actions taken to reach their goal. In addition, suggestions for improving nutrition and diabetes management will be reviewed. For this purpose, the information entered by the participants in their diary will be used and a short questionnaire oriented to self-report adherence, physical activity and dietary changes will be administered.
- ***If they did not reach the goal:*** They will be asked about the actions taken to lose weight and the main challenges to implement them. For this purpose, the information entered by the participants in their diary will be used. Suggestions for improving nutrition and diabetes management will be reviewed. In addition, a short questionnaire oriented to self-report adherence, physical activity and dietary changes will be administered.
- In session 7 a blood sample will be collected to measure his/her Hba1c. The results will be given in session 8 (last session) in which he/she will be rewarded if his/her Hba1c has dropped at least 1% since the beginning of the study, and if his/her companion has been with him/her.

Phase 3: Follow-up of experiences with the research study

In-depth interviews will be used with study participants. To (a) explore their opinion about the impact of having received financial incentives to lose weight and thus improve their diabetes management; (b) explore their opinion about the amount of the incentive, to find out if it was considered high, very low or reasonable, (c) find out their opinions about the educational material received (d) find out (in arm 2) the role played by the companions and document the different ways in which they supported the patient to reach his/her goals.

Procedures: Interviews will be conducted by personnel appropriately trained in qualitative techniques. Interviews will be audio-recorded and transcribed verbatim. Transcripts will be coded according to themes using ATLAS.ti version 7 for Windows.

Sample size: 30 people.

- 18 participants; 6 from the individual incentive arm, 6 from the researcher-determined mixed incentive arm, and 6 from the participant-determined mixed incentive arm.
- 12 companions: 6 from each arm.

3.7. Communicating results to patients

Hba1c, blood pressure, and weight results will be communicated and given to participants by the diabetes educator of the study. Participants will be advised, if necessary, to consult their attending physician for proper interpretation of the results.

3.8. Timeline

Research activities	MONTHS									
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Protocol preparation	x									
Ethics approval		x	x							
Recruitment				x	x					
Intervention					x	x	x	x		
Qualitative assessment								x	x	
Interview transcription									x	
Data analysis						x	x	x		
Final report writing										x

4. PROTECTION OF HUMAN SUBJECTS

4.7. Ethics

This protocol, questionnaires and informed consents - and any subsequent modifications - will be reviewed and approved by the Comité Institucional de Ética - CIE (Institutional Ethics Committee) of the Hospital Nacional Arzobispo Loayza with regard to their scientific content and compliance related to research on human subjects.

4.8. Informed Consent

Before providing informed consent, participants will be given the opportunity to ask questions until they fully understand the study. The interviewer will sign the guide to informed consent and give a copy to the interviewee (See Annex 4).

All participants will be assigned a unique identification code. Data will be stored in paper and electronic form. Electronic data will be archived, copied and secured with passwords. Paper forms will be stored in locked cabinets with access limited to specific individuals. Personal information, including the participant's name, address, date of birth, and other potential identifiers will be stored in password-protected folders. Only study staff will have access to this information.

4.9. Benefits

Participants may benefit from the financial incentives they receive and from the education and medical test results provided during their participation. This research study is subsequently for the participant to use the incentives for improvement and control of his/her disease.

4.10. Risks

No major security issues are expected in this study. Transportation costs, if necessary, will be covered by the project.

4.11. Payment to participants

Participants will not receive payment for participating in this study. They will receive a financial incentive for reaching certain weight loss and diabetes management goals.

4.12. Confidentiality

All information related to the study will be stored securely. All participant information will be stored in password-protected databases on computers accessible only to study investigators. All reports, study data, processes, and administrative forms will be identified only by a numeric code to maintain confidentiality. All information resulting from this research study will be treated with strict confidentiality, and only the investigators named in this study, local regulatory authorities, Ethics Committees, and those they designate will have access to this information.

Findings of this study will be submitted by the investigators to peer-reviewed indexed journals for publication.

5. DATA MANAGEMENT AND ANALYSIS PLAN

5.7. Data Security and Quality Control

A multi-faceted program for data quality control of the study that includes: (1) daily meetings and reviews with field interviewers for quality control as well as training updates, (2) duplicate data entry into a revenue-related database and that has automatic monitors for data validity, and (3) a continuous review of the statistical description of study data by the Principal Investigator is proposed.

Field visits will be conducted during the study to ensure that regulatory requirements are met. Data security includes physical security of paper-based formats and computers used for the study, as well as password protection and a backup of all information on the computers.

The close cooperation of the study investigator, field interviewers, data managers, and other members of the research team will be necessary to follow the progress of the study, answer questions about the proper execution of the study, and address other issues in a timely manner.

5.8. Analysis Plan

5.8.1. Baseline and Follow-up

The information collected will be entered and tabulated in order to identify the participants' characteristics. Subsequently, the data will be descriptively analyzed using measures of central tendency, measures of dispersion, absolute frequencies and relative frequencies, according to the type of variable.

For longitudinal data analysis, the three arms of the study (individual incentives, mixed incentives set up by researchers, mixed incentives set up by participants) will be compared, using as outcomes the difference in weight (every 15 days for three months) and the difference in the percentage of glycated hemoglobin (at three months). For this purpose, relative risks with 95% confidence intervals will be used.

5.8.2. Qualitative Research: In-depth interviews. The interviews will be recorded in mp3, transcribed and then analyzed using Atlas-ti software. This software allows coding the interviews in order to identify common themes, frequency of opinions and explanatory details of the answers given.

5.9. Protocol compliance

This research study will be carried out in accordance with the protocol and good clinical practices. The protocol will not be amended without prior written approval by the Ethics Committee. All amendments will be submitted for evaluation to institutional ethics committees prior to their implementation, except when it is necessary to protect the participants' security, rights or welfare, or to eliminate immediate risks to them.

5.10. Data security plan

Data management will follow standards of good clinical practice. We will follow standard procedures and definitions for the evaluation and reporting of adverse events. The Principal Investigator will be responsible for reporting all adverse events that are observed or reported during the study. All study personnel will be instructed to detect and report any adverse events. The Principal Investigator will be responsible for centralizing all this information.

6. REFERENCES

1. Lazo MdL, Loza J, de la Cruz C, et al. Quality of metabolic control in ambulatory type 2 diabetes patients under a challenging health system for chronic diseases. Global health, epidemiology and genomics. Submitted 2016.
2. Lerner AG, Bernabe-Ortiz A, Gilman RH, Smeeth L, Miranda JJ. The "Rule of Halves" Does Not Apply in Peru: Awareness, Treatment, and Control of Hypertension and Diabetes in Rural, Urban, and Rural-to-Urban Migrants. Critical pathways in cardiology 2013;12:53-8.
3. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993;329:977-86.
4. Goldman DP, Zheng Y, Girosi F, et al. The benefits of risk factor prevention in Americans aged 51 years and older. Am J Public Health 2009;99:2096-101.
5. Silva H, Hernandez-Hernandez R, Vinueza R, et al. Cardiovascular risk awareness, treatment, and control in urban Latin America. American journal of therapeutics 2010;17:159-66.
6. Gneezy U, Meier S, Rey-Biel P. When and Why Incentives (Don't) Work to Modify Behavior. . Journal of Economic Perspectives 2011;25:191-210.
7. Halpern SD, Madison KM, Volpp KG. Patients as mercenaries?: the ethics of using financial incentives in the war on unhealthy behaviors. Circ Cardiovasc Qual Outcomes. 2009 Sep2(5):514-6
8. Becker GS, Murphy KM. A Theory of Rational Addiction. Journal of Political Economy 1988;96:675-700
9. Volpp KG, Pauly MV, Loewenstein G, Bangsberg D. P4P4P: an agenda for research on pay-for-performance for patients. Health affairs 2009;28:206-14.
10. O' Donoghue T, Rabin M. Doing it Now or Later. American Economic Review 1999;89:103-24.
11. O' Donoghue T, Rabin M. Choice and Procrastination. Quarterly Journal of Economics 2001;116:103-60.
12. Sindelar JL. Paying for performance: the power of incentives over habits. Health economics 2008;17:449-51.
13. Volpp KG, John LK, Troxel AB, Norton L, Fassbender J, Loewenstein G. Financial incentive-based approaches for weight loss: a randomized trial. JAMA 2008;300:2631-7.
14. Volpp KG, Troxel AB, Pauly MV, et al. A randomized, controlled trial of financial incentives for smoking cessation. N Engl J Med 2009;360:699-709.
15. Gneezy U, Rustichini A. Pay enough or don't pay at all. The Quarterly Journal of Economics

2000;115:791-810.

16. Ariely D, Bracha A, Meier S. Doing good or doing well? Image motivation and monetary incentives in behaving prosocially. The American Economic Review, 2009;991.
17. Lacetera N, Macis M. Do all material incentives for pro-social activities backfire? The response to cash and non-cash incentives for blood donations. Journal of Economic Psychology 2010;31:738-48.
18. Kane RL, Johnson PE, Town RJ, et al. Economic Incentives for Preventive Care. Summary, Evidence Report/Technology Assessment: Number 101. AHRQ Publication Number 04E0241, August 2004. Agency for Healthcare Research and Quality, Rockville, MD
19. Lacetera N, Macis M, Slonim R. Will there be blood? Incentives and displacement effects in pro-social behavior. American Economic Journal: Economic Policy 2012;4:186-223.
20. S H, MM K, Y. W. Analyzing compensation methods in manufacturing: Piece rates, time rates or gain-sharing? NBER working paper: #16540 2010.
21. Tsai AG, Wadden TA. Systematic review: an evaluation of major commercial weight loss programs in the United States. Ann Intern Med 2005;142:56-66.
22. Long JA, Jahnle EC, Richardson DM, Loewenstein G, Volpp KG. Peer mentoring and financial incentives to improve glucose control in African American veterans: a randomized trial. Ann Intern Med 2012;156:416-24.
23. Lorincz IS, Lawson BC, Long JA. Provider and patient directed financial incentives to improve care and outcomes for patients with diabetes. Current diabetes reports 2013;13:188-95.
24. Lagarde M, Haines A, Palmer N. The impact of conditional cash transfers on health outcomes and use of health services in low and middle income countries. Cochrane database of systematic reviews 2009:CD008137.
25. Fernald LC, Gertler PJ, Neufeld LM. Role of cash in conditional cash transfer programmes for child health, growth, and development: an analysis of Mexico's Oportunidades. Lancet 2008;371:828-37.
26. Perova E, Vakis R. Welfare impacts of the “Juntos” Program in Peru: Evidence from a non-experimental evaluation The World Bank; 2009.
27. Trujillo A, Fleisher L. Beyond Income, Access and Knowledge: the Education Gradient on Prevention among Diabetics and Hypertensive. Aging and Health 2013.
28. Sloan FA, Padron NA, Platt AC. Preferences, beliefs, and self-management of diabetes. Health services research 2009;44:1068-87.
29. The effect of intensive treatment of diabetes on the development and progression of long-term complications in insulin-dependent diabetes mellitus. The Diabetes Control and Complications Trial Research Group. N Engl J Med 1993;329:977-86.

30. Klonoff D, Schwartz D. An economic of interventions for diabetes. Diabetes Care 23:390-404, 2000.
31. Miranda JJ, Bernabe-Ortiz A, Smeeth L, Gilman RH, Checkley W. Addressing geographical variation in the progression of non-communicable diseases in Peru: the CRONICAS cohort study protocol. *BMJ open* 2012; **2**(1): e000610.
32. Chobanian, A. V., G. L. Bakris, H. R. Black, W. C. Cushman, L. A. Green, J. L. Izzo, Jr., D. W. Jones, B. J. Materson, S. Oparil, J. T. Wright, Jr., E. J. Roccella, L. National Heart, D. E. Blood Institute Joint National Committee on Prevention, P. Treatment of High Blood and C. National High Blood Pressure Education Program Coordinating (2003). "The Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report." JAMA 289(19): 2560-2572.
33. Flores Juan C, Alvo M, Borja H, Morales J, Vega J, Zúñiga C. Enfermedad renal crónica: Clasificación, identificación, manejo y complicaciones. Rev. médica Chile [Revista en Internet]. 2009 Enero [Citado 2015 Feb 17]; 137(1): 137-177.
34. Bloom S, Till S, Sonksen P, Smith S: Use of biothesiometer to measure individual vibration perception thresholds and their variation in 519 non-diabetic subjects. *Br Med J* 288:1793–1795,1984
35. Young MJ, Breddy JL, Veves A, Boulton AJ: The prediction of neuropathic foot ulceration using vibration perception thresholds: a prospective study. *Diabetes Care* 17:557–560, 1994
36. "PanOptic," www.welchallyn. comlpromotions/PanOptic/default.htm.
37. G. Bradski, "The OpenCV Library," Dr. Dobb's Journal of Software Tools, 2000.
38. Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 statement: updated guidelines for reporting parallel group randomised trials. PLoS Med 2010;7:e1000251.