SPECIAL COLLABORATION

COHORT STUDY IN PRIMARY HEALTH CARE ON THE EVOLUTION OF PATIENTS WITH PREDIABETES (PREDAPS). BASIS AND METHODOLOGY (*)

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ABSTRACT

The PREDAPS study aims to determine the risk of developing diabetes and the risk of vascular complications in patients with prediabetes and identify factors associated with those risks. It is a prospective observational study of a cohort of 1184 subjects with prediabetes and another cohort of 838 subjects with no alterations in glucose metabolism. The data at baseline were obtained from patients attending primary care centers in Spain throughout 2012. Subjects with prediabetes were classified into three groups: those who had only altered the fasting blood glucose levels -between 100 and 125mg/dl-, those who had only altered the HbA1c level -between 5.7 and 6.4% - and those who had altered both parameters. Information on sociodemographic characteristics, personal and family history, lifestyle and drug therapy was obtained from medical records and the interview with the doctor in the consultation. It was also performed a physical examination to determine weight, height, waist circumference and blood pressure were performed and blood and urine analysis. The PREDAPS study may help to reduce uncertainty in individual prevention strategies in subjects with prediabetes. Annual monitoring of patients recruited for five years will enable to know the risk of developing diabetes type 2 and the risk of macro-and microvascular complications in the three groups of subjects with prediabetes and determine the factors associated with those risks.

Palabras clave: Diabetes mellitus. Prediabetic state. Diabetes Mellitus, Type 2study. Diabetes complications. Cohort studies.Prospective Studies. HbA1c.

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RESUMEN

Estudio de cohortes en atención primaria sobre la evolución de sujetos con prediabetes(PREDAPS). Fundamentos y metodología

El estudio PREDAPS pretende determinar el riesgo de desarrollo de diabetes y aparición de complicaciones vasculares en sujetos conprediabetes e identificar los factores asociados. Se trata de un estudio observacional de seguimiento de una cohorte de 1.184 sujetos con prediabetes y otra cohorte de 838 sujetos sin alteraciones en el metabolismo de la glucosa. Los datos de la etapa basal se obtuvieron de pacientes que acudieron a centros de Atención Primaria en España a lo largo del año 2012.Los sujetos con prediabetes fueron clasificados en tres grupos: los que solo tenían alteradas las cifras de glucemia en ayunas -entre 100 y 125 mg/dl-, los que solo tenían alterado el nivel de HbA1c -entre 5,7 y 6,4%- y los que tenían alterados ambos parámetros. La información sobre sus características sociodemográficas, antecedentes familiares y personales, estilos de vida y tratamiento farmacológico se obtuvo de la historia clínica y de la entrevista realizada en la consulta por el médico. Se realizó un examen físico para determinar peso, talla, perímetro de la cintura y presión arterial y se realizaron análisis de sangre y orina. El estudio PREDAPS puede contribuir a disminuir la incertidumbre en las estrategias individuales de prevención en los sujetos con prediabetes. El seguimiento anual durante cinco años de los participantes posibilitará conocer el riesgo de desarrollo de diabetes mellitus tipo 2 y el de complicaciones macro y microvasculares en los tres grupos de sujetos con prediabetes, así como averiguar los posibles factores asociados a esos riesgos.

Keywords: Diabetes mellitus. Prediabetes. Complicaciones de la diabetes. Estudio de cohortes. Estudio prospectivo. Hemoglobina A Glicosilada.

INTRODUCTION

According to the International Diabetes Federation, in 2011 around 366 million persons worldwide aged 20 to 79 years suffered from diabetes mellitus[1]: 90% suffered from diabetes mellitus type 2 (DM2), a potentially preventable disease, inasmuch as its development is associated with the presence of social and lifestyle factors. The 2009 European Health Survey[2] estimated the prevalence of DM2 to be 8% in the European Union and 6.4% in Spain. Nevertheless, the most recent epidemiological studies, based on diagnosed DM2, put its prevalence between 10% and 15%.[3-4]

Patients with DM2 have a higher coronary risk than does the general population and a high risk of suffering from microvascular complications, such as retinopathy, nephropathy and peripheral neuropathy.[3] Consequently, persons with diabetes undergo a greater number of hospitalisations, a higher rate of readmissions and a longer duration of hospital stay than does the population without diabetes. Cardiovascular complications are the main reason for the increase in hospital morbidity.[2] In Spain, patients with DM2 visit their general practitioner 8 to 9 times per year[5] and the related cost is practically double that of patients without diabetes.[6]

In view of the high social and health-care burden generated by DM2, the findings of some studies have raised hope about the possibility of alleviating the impact of this health problem on the population, by highlighting the fact that it might be possible to prevent or delay the onset of the disease through changes in lifestyle and/or drugs therapy.[7-10] These findings are of extraordinary relevance, since it would be possible to know which individuals had a high risk of diabetes mellitus, with a view to planning the pertinent prevention strategies.

As progression from normality to DM2 can last several years, it is essential to identify prediabetic states. Prediabetes, defined by blood glucose concentrations that are higher than normal but lower than the thresholds established for diagnosis of diabetes, is a high-risk state for development of DM2. According to the World Health Organisation, persons have a high risk of developing DM2 if they present with either of the following two states: impaired fasting glucose (IFG), if fasting glucose concentrations lie between 110 and 125 mg/dl; or impaired glucose tolerance (IGT), if glucose concentrations lie between 140 and 200 mg/dl two hours after an 75 gr. oral glucose overload.[11] The American Diabetes Association (ADA) set the same thresholds for IGT, decided to reduce the lower limit for definition of IFG to 100 mg/dl, and introduced glycated haemoglobin (HbA1c) of 5.7% to 6.4% as a new high risk category of developing DM2.[12]

Around 5% to 10% of persons with prediabetes develop diabetes every year, and 70% will develop diabetes over their lifetimes.[13] Spanish studies on DM2 incidence among subjects with prediabetes[14-16] have reported lower figures than studies undertaken in other countries.[17-18] This difference may be due to the fact that the Spanish studies used samples of subjects drawn from the general population, whereas many studies conducted outside Spain have studied subjects selected from routine clinical practice, thereby rendering the presence of individuals with impaired glucose metabolism more likely. It is therefore important to conduct a study in Spain which assesses the incidence of diabetes in prediabetic patients identified in routine medical practice, in order to ascertain whether the frequency of appearance of diabetes is similar to that observed in other countries.

It should also be stressed that hardly any studies have attempted to ascertain which factors increase the risk of developing DM2 among subjects with prediabetes. Indeed, one such study was conducted in Spain on a sample of 115 patients with IFG,[19] with only obesity showing a statistically signifi-

cant association with the risk of ocurrence of DM2. Generating evidence that served to reduce this gap in knowledge would be useful for clinical practice. Only by knowing the factors that are associated with progression to DM2 or changes in its levels, will it be it possible to make a prognosis and implement more appropriate interventions for each subject.

Furthermore, prediabetes is also associated with a higher frequency of appearance of cardiovascular complications, and kidney and neurological disorders.[13] Since DM2 is a risk factor for major cardiovascular diseases, it is not sufficiently clear whether this increase in risk occurs before the development of clinical diabetes mellitus or after its onset.[20-21]

OBJECTIVES

The Cohort study in Primary Health Care on the Evolution of Patients with Prediabetes (Evolución de patients con prediabetes en Atención Primaria de Salud - PREDAPS) is to ascertain the incidence of diabetes mellitus and the ocurrence of cardiovascular complications in subjects with prediabetes, and identify related factors. This study also seeks to identify the factors that are associated with the risk of onset of these health problems among individuals who are prediabetic versus those without impaired glucose metabolism. .

SUBJECTS AND METHODS

Design. This is a prospective cohort study in which one cohort of subjects with prediabetes and another of subjects without impaired glucose metabolism will be followed up for a minimum of 5 years. Baseline stage data were collected from February to November 2012. Data were collected during routine clinical practice by general practitioners from patients attending primary health care (PHC) facilities nation-wide.

A data-collection questionnaire was purpose-designed to enable general practitioners to complete and submit it telematically. During the course of November 2011, five physicians took part in a pilot test in the place of medical consultation to detect possible problems in patient-selection and the suitability of the questionnaire, i.e., in terms of comprehension by both physician and patient, and possible problems in filling and handling of the electronic platform that served as support for data entry. In December 2011, the regional co-ordinators of the study reached an agreement about the procedure to be followed for patient selection. In addition, they proposed some modifications to the electronic platform to make it more user-friendly and simpler for answering the questionnaire.

In January 2012, a meeting was held with all the general practitioners who had previously consented to participate as researchers. At this meeting, they were given a protocol with the data-collection questionnaire, informed consent form and participant-selection criteria. The questionnaire with the different variables was explained to them and any doubts raised were addressed. In addition, a demonstration was given of how the electronic data-collection platform operated, and a sealed envelope was handed out containing the personal user code and access password. The platform is housed on the website, www.redgdps.org, which is hosted by the Consortium of Primary Care Diabetes Study Groups (Red de Grupos de Estudio de la Diabetes en Atención Primaria de Salud - redGDPS). A total of 125 general practitioners recruited the study participants.

Participants were required to sign the informed consent form provided to them by the researchers. The study was classified by the Spanish Drug and Health Product Agency (Agencia Española de Medicamentos y Productos Sanitarios) as a Non-Interventional (Observational) Post-Authorization Study, and the protocol was approved by the Parc de Salut Mar Clinical Research Ethics Committee in Barcelona.

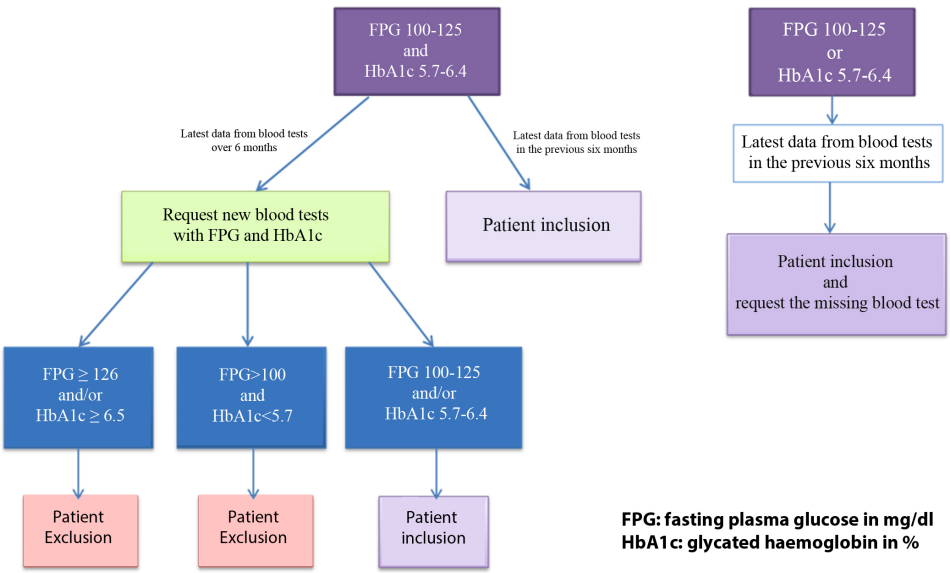
Study subjects. The study population consisted of patients who attended the PHC facilities at which the researchers worked. The inclusion criteria for the cohort of prediabetic subjects were: age 29 years to 75 years; and presence of one of the following two values in the preceding six months, namely, most recent fasting plama glucose (FPG) value of 100 mg/dl to 125 mg/dl, or most recent HbA1c value of 5.7% to 6.4%. Patients who consecutively attended their physicians' surgeries for any reason and met the inclusion criteria were invited by the researchers to participate in the study. Patients who met the ADA criteria for classification as prediabetic on the basis of their clinical histories but had not undergone any analysis in the preceding six months, underwent one to assess whether or not they should be included in the study. The exclusion criterion was presence of any of the following processes: diabetes mellitus; terminal diseases; pregnancy; major surgery or hospital admission in the preceding 3 months; or any haematological disease that might interfere with HbA1c values. The strategy for inclusion of patients in the cohort of subjects with prediabetes is depicted in figure 1.

To determine the sample size, authors reviewed studies addressing the frequency of conversion of prediabetes to DM2.[14-15,22-24] In the light of the disparity in their results, and in order to ensure the most unfavourable situation from the standpoint of the number of subjects required, the lowest conversion frequency estimates were taken as reference. To this end, the result of Heianza et al's study was used,[24] which followed up 2,092 prediabetic subjects for a mean of 4.7 years and found a DM2 incidence of 30 per 1,000 person-years. This figure means that approximately 15% of subjects with prediabetes will develop DM2 in the first five years of follow-up. Accordingly, the number of individuals needed to detect a relative difference of 50% (relative risk of 1.5) within this time frame, between subjects with a given risk factor and those who do not have it, would be 1,450, assuming an incidence of 10% among unexposed persons, the same number of individuals in each of the two categories of the risk factor, an α error of 0.05, and a power (1- β) of 0.80. Because a loss to follow-up of 10% was envisaged, the estimated number of subjects with prediabetes to be included in the study was 1,600. Finally, 1,184 patients with prediabetes were selected, 74% of the initially envisaged total. Table 1 shows that 21.5% of these patients had FPG of 100 mg/dl to 125 mg/dl, 26.7% had HbA1c of 5.7% to 6.4%, and 51.9% presented with both impairments. This finding differs from the study by Heianza et al,[24] in which 60% of patients were prediabetic as per the IFG criterion, 20% as per the HbA1 criterion, and 20% as per both criteria. In view of the fact that the DM2 conversion rate is almost 5 times higher in subjects who have two as opposed to one impairment,[24] incidence of DM2 in the PREDAPS study would foreseeably be higher than 30 per 1000 person-years, the figure reported by the latter study. This fact would lead to an increase in the statistical power of the study with respect to the initially planned and therefore would compensate the smaller sample size.

In the cohort of subjects without impaired glucose metabolism, patients in the same age range were include who did not meet either of the two criteria that defined the cohort of subjects with prediabetes in terms of FPG and HbA1c. The strategy for including patients in this cohort of subjects is depicted in figure 2. The exclusion criteria were the same as those for the cohort of subjects with prediabetes. Table 2 shows the sociodemographic characteristics of subjects with prediabetes and subjects without impaired glucose metabolism.

The initial plan was to include the same number of individuals in both cohorts. Whenever a prediabetic patient consented to par-

Figure 1
Strategy for inclusion in the cohort of subjects with prediabetes

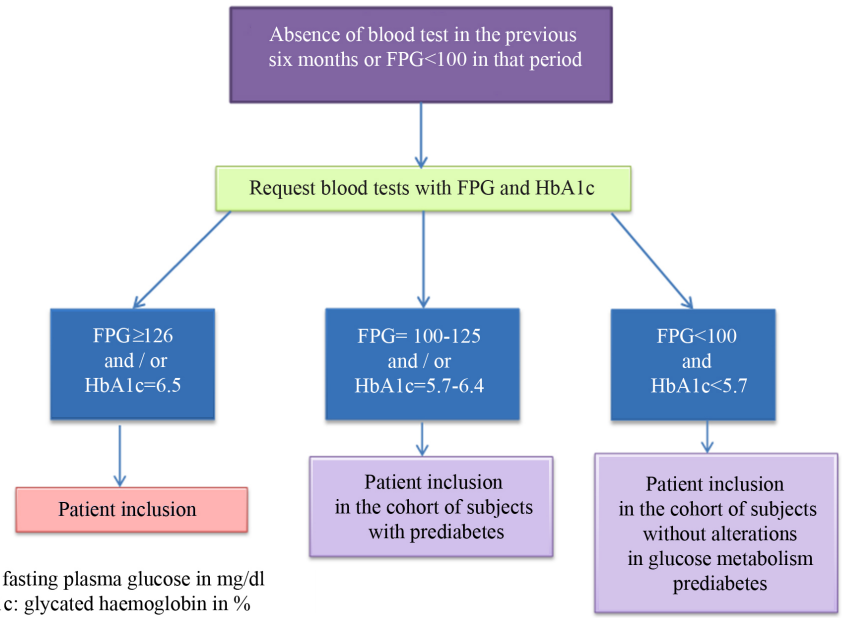


ticipate in the study, the next patient of the same sex and age ± 5 years who presented with baseline glycaemia of under 100 mg/dl, was invited by the physician to participate. If he/she consented to take part, an HbA1c reading was taken. Only in cases where the patient's HbA1c was under 5.7%, was he/she included in the cohort of subjects without impaired glucose metabolism. During this stage of patient enrolment, an unexpected event occurred however: on determining HbA1c, around 40% of these patients presented with HbA1c readings ranging from 5.7% to 6.4%, so that they went to form part of the cohort of subjects with prediabetes. This circumstance made it difficult to obtain a ratio of 1:1 between the two cohorts. The final number of individuals included in the cohort of subjects without impaired glucose metabolism was 838, amounting to a ratio of 1.4:1. Assuming a 1.5% occurrence of DM2 and / or a cardiovascular event during the five year follow-up in these patients, it will be possible to identify a relative risk of 2.5 or

Table 1
Distribution of prediabetic subjects by type of impaired parameter

Parameter	n	%
Glycaemia 100-125 mgr/dl and HBA1c <5.7 %	254	21.5
Glycaemia < 100 mgr/dl and HBA1c 5.7%-6.4%	316	26.7
Glycaemia 100-125 mgr/dl and HBA1c 5.7%-6.4 %	614	51.9
Total	1,184	100.00

Figure 2
Strategy for inclusion in the cohort of subjects without alterations in glucose metabolism prediabeteslism, according to different socio-demographic variables



FPG: fasting plasma glucose in mg/dl
HbA1c: glycated haemoglobin in %

greater to compare the development of these health problems in subjects with prediabetes in realtion to subjects without alteration in the metabolism of glucose.

Study variables and data-collection. The variables measured in the PREDAPS study are listed in Appendices 2 and 3. The questionnaire included questions drawn from health surveys and epidemiological studies undertaken in Spain. A copy of the questionnaire can be obtained by accessing the website: www.redgdps.org.

Information on biographical data, family history, personal history, lifestyle, drug treatment, social support and socioeconomic position were obtained from each participant's clinical history and from the personal interview conducted by the physician at his/her surgery. During the medical visit, a physical examination was performed, which included anthropometry, and determination of blood pressure and heart rate. Similarly, a blood and urine analysis was requested to determine FPG, HbA1c, lipid profile, transaminase, haemogram, iron levels and kidney function (plasma creatinine, glomerular filtration, albuminuria and albumin/creatinine ration in early morning urine). In subsequent annual follow-ups, the information to be recorded is that which allows to know the changes that have occurred in the different variables with respect to the baseline.

During the data-collection period at baseline, validation procedures were periodically conducted on the information recorded in the e-platform, in order to identify possible inconsistencies and verify that patients met the inclusion criteria. The physicians

Table 2
Distribution of subjects with prediabetes and subjects without impaired glucose metabolism, according to different socio-demographic variables

Sociodemographic characteristics	Subjects with prediabetes						Subjects without impaired glucose metabolism	
	Impaired baseline glycaemia[a]		Impaired HBA1c[†]		Both parameters impaired[‡]			
	n	%	n	%	n	%	n	%
Total	254	100.0	316	100.0	614	100.0	838	100.0
Sex								
Men	156	61.4	126	39.9	313	51.0	388	46.3
Women	98	38.6	190	60.1	301	49.0	450	53.7
Age (years)								
30-49	58	22.8	55	17.4	74	12.1	201	24.0
50-59	80	31.5	95	30.1	186	30.3	257	30.7
60-74	116	45.7	166	52.5	354	57.7	380	45.3
Educational level								
Primary or lower	115	45.3	163	64.2	339	51.8	386	46.1
Secondary, 1st stage	35	13.8	37	14.6	75	11.5	85	10.1
Secondary, 2nd stage	67	26.4	63	24.8	121	18.5	202	24.1
University	37	14.6	53	20.9	79	12.1	165	19.7
Marital status								
Single	11	4.3	42	16.5	46	7.0	87	10.4
Married	219	86.2	231	90.9	478	73.1	645	77.0
Separated	16	6.3	24	9.4	37	5.7	55	6.6
Widowed	8	3.1	19	7.5	53	8.1	51	6.1

[*]Glycaemia 100-125 mgr/dl and HBA1c <5.7 % . [†] Glycaemia <100 mgr/dl and HBA1c 5.7%-6.4% .
[‡]Glycaemia 100-125 mgr/dl and HBA1c 5.7%-6.4%

responsible were notified of any problems detected, so that they could proceed to remedy these and/or the replace any patients who failed to meet the criteria.

Statistical analysis. Statistical analyses will be performed in accordance with the plan drawn up in the protocol for addressing the main study objectives. Firstly, the information collected at baseline will make it possible to ascertain whether the risk of developing DM2 is higher among subjects with prediabetes than among those without impaired glucose metabolism. The prevalence of risk factors for development of diabetes in both cohorts will be calculated. Since the cohort of subjects without impaired glucose metabolism is younger (as can be seen from table 2), age-adjusted prevalence will be computed.

At five years of follow-up, an analysis will be performed covering all the study subjects as a whole to examine the possible association between family and personal history, lifestyle, anthropometric measures and biochemical parameters on the one hand, and incidence of DM2 and vascular complications on the other. The measure of association used will be the hazard ratio (HR), calculated using Cox regression.

Subsequently, the incidence of DM2 and vascular complications will be calculated in both cohorts. Since the factors associated with development of DM2 will foreseeably display a different distribution in the two cohorts, age- and sex-adjusted incidence will first be calculated separately for the respective cohorts, after which the increase in the risk of ocurrence of diabetes and

vascular complications will be calculated in the prediabetic cohort with respect to the cohort without impaired glucose metabolism. The measure of association used will be the HR, calculated using Cox regression. The overall HR will be estimated, and a multivariate analysis will then be performed to control for any possible confounding that might have been introduced into the estimates by the different distribution of the various characteristics in the two cohorts. Control for age and sex will be followed by the successive inclusion of socio-economic characteristics, drug treatment, family and personal history, lifestyle and anthropometric measures. This will enable to establish which factor contributes most to the probable increase in risk in the cohort of prediabetic subjects with respect to that of subjects without impaired glucose metabolism.

DISCUSSION

The use of the HbA1c criterion, in addition to the IFG criterion, in the PREDAPS study has allowed to identify different groups of subjects with prediabetes. This will, in turn, make it possible to establish the risk of developing diabetes and vascular complications, as well as ascertain the possible related factors in each group.

The results of various studies show that HbA1c identifies a smaller proportion of prediabetic patients than does IFG.[25] For instance, in studies undertaken in the USA[26] and Japan[24] around 60% of patients with prediabetes were diagnosed as having IFG but not HbA1c impaired, close on 20% were diagnosed as having HbA1c but not IFG impaired, and around 20% were diagnosed as having both parameters impaired. In the PREDAPS study, however, the findings have been different: approximately half of the patients had both parameters impaired. Similar results were obtained in a population in southern China[27] and are in line with HbA1c possessing a greater sensitivity than IFG for diagnosis of diabetes in Spain.[28]

Although the variation in the percentage of prediabetic subjects identified on the basis of HbA1c has been reported related to subjects' ethnic origin,[24] it is likely that other characteristics inherent in prediabetes may account for the heterogeneity of the findings. Indeed, in all the studies undertaken around the world, a strong concordance between IFG and HbA1c has been observed for diagnosis of DM2, as compared to the moderate correlation observed for diagnosis of prediabetes.[26,29-31]

Some authors have criticised the use of HbA1c because it classifies healthy subjects as subjects with prediabetes.[32-33] This criticism is based on its foreseeable negligible effectiveness for tackling individual prevention of diabetes mellitus, since the establishment of lifestyle changes and use of hypoglycaemiant agents in such subjects may entail enormous costs for health-care systems. Nevertheless, the results of a number of studies appear to support the ADA's recommendation to use HbA1c to identify subjects with prediabetes with a view to individual prevention strategies, since such patients have a high risk of developing DM2.[34-35] Furthermore, some findings suggest that HbA1c also predicts the onset of vascular complications in nondiabetic subjects.[35]

In contrast, the PREDAPS study did not include subjects with prediabetes based on abnormal glucose tolerance, whose physiopathological characteristics (muscular resistance to insulin accompanied by defective early- and late-phase secretion) are different to those of subjects with IFG[36] (hepatic resistance to insulin accompanied by defective early-phase secretion), though they have a similar risk of developing DM2.[18,37] Moreover, the risk is higher if subjects present with both IFG and glucose intolerance.[18,37] The inclusion of such subjects was rejected because it increased the complexity of the study and could be a barrier to adherence of researchers involved in the recruitment of subjects and data collection.

The most noteworthy aspect of the baseline stage of the PREDAPS study was the great difficulty experienced by researchers in including persons without impaired glucose metabolism. This circumstance reflects the high prevalence of prediabetes in the Spanish population and underscores the pertinence of conducting this study. Another consequence of this factor was the impossibility of successfully matching the two cohorts of subjects by age, since the cohort without impaired glucose metabolism was younger. Therefore, any analysis comparing the two cohorts in both the findings of the baseline period as the health problems occurring during the follow-up should include age as a variable of adjustment.

The data-collection form included the fact of patients taking medication, including oral antidiabetics. Altgough there is no agreement among different authors about the use of these drugs in prediabetic subjects to prevent the ocurrence of DM2 and cardiovascular complications, this may be the therapeutic attitude of some researchers. In the findings obtained in the future should consider this fact. In any case, only nine of the 1,184 patients with prediabetes were undergoing treatment with oral antidiabetics.

It is important to mention that the PREDAPS study highlights the feasibility of conducting an observational study, with data collected nation-wide by primary care physicians during routine clinical practice. The inclusion rate of patients with respect to the originally planned was higher than in other studies of similar design. The key to this success was the enthusiastic response of physicians to the invitation extended by the redGDPS to take part in the study.

Lastly, another strength of the PREDAPS study was its standardised collection of data on risk factors and other variables using a pre-established protocol. However, the measurements taken during the physical examination were made with instruments available to the respective physicians at their surgeries, and the analytical determinations were performed at different laboratories. This entails the possibility of an information bias in the classification of certain patients in the categories established by these variables. Even so, this would be a nondifferential bias with respect to incidence of health problems, since it is unlikely that the ocurrence of DM2 and/or vascular complications in the respective patients is related to the instruments used or the methods employed by specific laboratories.

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Appendix 1
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Appendix 2
Types of data and main study variables collected by personal interview or from patients' clinical history

Biographical data Age, sex, place of birth, town and province of residence
Family history Diabetes, arterial hypertension, ischaemic heart disease, stroke, hypercholesterolaemia, sudden death (parents, children or siblings)
Personal history Hypertriglyceridaemia, hypercholesterolaemia, arterial hypertension, macrovascular and microvascular events, weight and order of birth. In women the following were also collected: number of births; birth weight of children; history of miscarriages; history of gestational diabetes; use of contraceptives and history of hormonal treatment for menopause
Diet Type of breakfast, eating between meals, frequency of consumption of a great variety of foods, intake of sweetened beverages
Smoking Presence or absence of habit (all), number of cigarettes per day and age at initiation (smokers and ex-smokers), and length of time during which the individual had quit smoking (ex-smokers).
Alcohol consumption Type of drinker (habitual, occasional, abstainer, ex-drinker), and frequency of consumption and amount consumed of a wide variety of drinks of differing alcoholic content. Physical activity Type of leisure-time physical activity (sedentary, occasional, moderate or intense) and weekly frequency of a wide range of physical activities, plus length of time spent on each occasion.
Pharmacological treatment Diuretics, ACE inhibitors, angiotensin II receptor antagonists, beta blockers, alpha blockers, direct acting arterial vasodilators, centrally acting antihypertensive agents, renin inhibitors, statins, ezetimibe, omega 3, nicotinic acid, fibrates, antiaggregants, oral anticoagulants, corticoids, neuroleptics, immunosupressors, thyroid antiretrovirals, hormones, anabolic hormones, oral antidiabetics.
Social network or support
Marital status, person(s) with whom subject cohabits, frequency of contact with family and friends.
Socio-economic position
Educational level, occupational status, occupation.

Appendix 3
Types of data and main study variables collected by physical examination or analytical determinations

Analytical test results

Fasting glucose
Glycated haemoglobin
DCCT, IFCC
Lipid profile:
Cholesterol, LDL, HDL, triglycerides
Uric acid
Transaminase GOT, GPT and GGT
Haemogram
Haemoglobin, MCV
Iron levels:
serum iron and ferritin
Kidney function.
Plasma creatinine, glomerular filtration, albuminuria and albumin/creatinine ratio in early morning urine

Physical examination

Blood pressure:
Systolic and diastolic blood pressure
Heart rate
Anthropometric measures:
Height, weight and waist circumference