Original article

Randomized Clinical Trial to Assess the Efficacy of a Comprehensive Programme of Secondary Prevention of Cardiovascular Disease in General Practice: The PREseAP Study

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ABSTRACT

Introduction and objectives: To assess the efficacy of a comprehensive program of secondary prevention of cardiovascular disease in general practice.
Methods: A cluster randomized clinical trial was carried out in a regular general practice setting. Male and female patients aged under 86 years with a diagnosis of ischaemic heart disease, stroke or peripheral artery disease were recruited between January 2004 and May 2005. Study participants were seen at 42 health centres throughout the whole of Spain. The primary endpoint was the combination of all-cause mortality and hospital cardiovascular readmission at 3-year follow-up.
Results: In total, 1224 patients were recruited: 624 in the intervention group and 600 in the control group. The primary endpoint was observed in 29.9% (95% confidence interval [CI], 25.5%–34.8%) in the intervention group and 25.6% (22.3%–29.2%) in the control group (P = .15). At the end of follow-up, 8.5% (6.3%–11.3%) in the intervention group and 11% (7.4%–16%) in the control group were smokers (P = .07). The mean waist circumference of patients in the intervention and control groups was 100.44 cm (95% CI, 98.97–101.91 cm) and 102.58 cm (95% CI, 100.96–104.21 cm), respectively (P = .07). Overall, 20.9% (15.6%–27.7%) of patients in the intervention group and 29.6% (23.9%–36.1%) in the control group suffered from anxiety (P = .05), and 29.6% (22.4%–37.9%) in the intervention group and 41.4% (35.8%–47.3%) in the control group had depression (P = .02).
Conclusions: A comprehensive program of secondary prevention of cardiovascular disease in general practice was not effective in reducing cardiovascular morbidity and mortality. However, some factors associated with a healthy lifestyle were improved and anxiety and depression were reduced.

Ensayo clínico aleatorizado para evaluar la eficacia de un programa integral de prevención secundaria de las enfermedades cardiovasculares en atención primaria: estudio PREseAP

RESUMEN

Introducción y objetivos: Evaluar la eficacia de un programa integral de prevención secundaria de las enfermedades cardiovasculares en atención primaria.
Métodos: Ensayo clínico aleatorizado, pragmático, por conglomerados realizado en atención primaria. Eran pacientes elegibles varones y mujeres menores de 86 años, diagnosticados de cardiopatía isquémica, accidente cerebrovascular o enfermedad arterial periférica entre enero de 2004 y mayo de 2005. Participaron en el estudio pacientes visitados en 42 centros de salud de todo el estado español. La variable de resultado fue la combinación de la mortalidad total y los reingresos hospitalarios por causa cardiovascular a los 3 años de seguimiento.

Resultados: Se reclutó a 1.224 pacientes, 624 en el grupo intervención y 600 en el grupo control. La variable principal de resultado se observó en el 29,9% (intervalo de confianza del 95%, 25,5-34,8) en el grupo intervención y en el 25,6% (22,3-29,2) en el grupo control (p = 0,15). Al final del seguimiento un 8,5% (6,3-11,3) del grupo intervención y un 11% (7,4-16) del grupo control eran fumadores (p = 0,07). El perímetro abdominal del grupo intervención fue 100,44 (98,97-101,91) cm y el del grupo control, 102,58 (100,96-104,21) cm (p = 0,07). El 20,9% (15,6-27,7) de los pacientes del grupo intervención y el 29,6% de los pacientes del grupo control (23,9-36,1) tenían ansiedad (p = 0,05), y el 29,6% (22,4-37,9) del grupo intervención y el 41,4% (35,8-47,3) del grupo control tenían depresión (p = 0,02).
Conclusiones: Un programa integral de prevención secundaria no es eficaz para reducir la morbimortalidad cardiovascular, pero sí en mejorar algunos aspectos relacionados con los hábitos saludables y en reducir la ansiedad y la depresión.

> **Abbreviations**
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> IHD: ischaemic heart disease
> PAD: peripheral artery disease
> IG: intervention group
> CG: control group

INTRODUCTION

The aim of secondary prevention strategies in patients with cardiovascular diseases is to reduce their risk of a new cardiovascular event and death and, therefore, to improve survival. It has been demonstrated that lifestyle changes, such as smoking cessation and a diet that modifies fatty acid profiles, lower cardiovascular morbidity and mortality in ischaemic patients and that physical exercise and cardiac rehabilitation after a myocardial infarction reduce the risk of cardiovascular deaths by 20%–25%. With respect to pharmacological treatment, we know that both prophylactic treatment and treatment designed to meet therapeutic objectives that target risk factors are beneficial.[1,2]

However, there are difficulties when it comes to incorporating the results of clinical trials into clinical practice. The comparison of the results of the EUROASPIRE I (1995–1996), EUROASPIRE II (1999–2000) and EUROASPIRE III (2006–2007) studies in patients with coronary disease show that the prevalence of risk factors continues to be high: smoking showed little variation (20.3%, 21.2%, and 18.2%), obesity (body mass index, BMI ≥ 30) increased from 25.0% to 32.6% and 38.0%, and poorly controlled blood pressure (BP) (BP ≥ 140/90 mm Hg) was scarcely modified (58.1%, 58.3%, and 60.9%). The only change was an important decrease in the prevalence of hypercholesterolaemia from 94.5% to 76.7% and 46.2%. As far as the use of prophylactic drugs is concerned, when the EUROASPIRE I and III studies[3–5] were compared, anti-platelet agents were seen to increase from 80.8% to 93.2%; the use of beta blockers from 56% to 85.5%; all antihypertensive drugs from 84.5% to 96.8% and hypolipaemic agents from 32.2% to 88.8%. Although certain improvements have been seen in these three studies over the years, there is still a significant percentage of patients in whom the control of risk factors could be improved. Studies conducted in our centres also showed that 54% of patients with a history of myocardial infarction had hypercholesterolaemia, 41% were hypertensive, 11% were smokers and 19% were obese. In addition, there was patent underuse of prophylactic medication.[6]

Recently, the results of a primary care study in Ireland were published. In this trial an intensive intervention was applied and 18 months later there was a reduction in the number of readmissions, but other clinical benefits were not observed.[7]

In our setting different initiatives have been adopted to improve secondary prevention in coronary patients. In the PRESENTE[8]

study, the implementation of a simple intervention programme in patients who were admitted with myocardial infarction was evaluated and an improvement was observed after 6 months of follow-up of blood pressure, lipids, weight and other lifestyle-related parameters. The ICAR study, which was carried out in Catalonia, assessed the efficacy of an intensive programme designed to achieve secondary prevention of heart disease and implemented by GPs themselves. An improvement in the control of blood pressure and an increase in HDL-cholesterol levels were obtained, but no reduction in cardiovascular morbidity and mortality was observed.[9,10]

The fundamental aim of this study is to evaluate whether an intervention in patients who have already been diagnosed with cardiovascular disease (ischaemic heart disease, stroke and peripheral arterial disease) at the primary care level in different autonomous communities is effective in reducing readmission of patients with cardiovascular pathology and total mortality. The secondary objectives are to evaluate whether the intervention is effective in controlling cardiovascular risk factors and the use of prophylactic drugs.

METHOD

The methodology for this study has already been described in previous articles.[11,12] Briefly, this is a randomized, pragmatic, cluster (health centres) clinical trial conducted at the primary care level. The health centres were randomly assigned to either continue delivering the care they routinely provided to patients diagnosed with cardiovascular disease (control group or CG) or to organize a specific secondary prevention unit (intervention group or IG). This study was registered in the International Clinical Trial Register (ISRCT No. 18578323).

The randomization was centralized at the Fundació Institut Català de Farmacologia of the Hospital Vall d'Hebron in Barcelona and the randomization sequence was not revealed until the intervention was assigned (*allocation concealment*). As a way of restricting the random assignment sequence, the study population was stratified into autonomous communities in order to ensure that the two study groups were representative of each community. The study was open-label so nothing was concealed from the investigators with respect to the group to which they were assigned nor was there any concealment in the evaluation of the results. The study was actively monitored by internal and external auditors in order to guarantee the quality of the data.

Study Subjects

Patients from eight autonomous communities throughout Spain, who attended 42 health centres participated in the study.

Criteria for Participation in the Study

Inclusion criteria: Men and women under 86 years of age and diagnosed between January 2004 and May 2005 with ischaemic cardiopathy (IC): acute myocardial infarction, unstable angina or acute coronary syndrome (confirmed by a hospital report), unstable angina confirmed by a diagnostic test (stress test and isotopic gammagraphy); cerebrovascular accident (CVA) verified by CT and/or a hospital report; and peripheral arterial disease (PAD) confirmed by ECHO Doppler or a positive ABI test.

Exclusion criteria: Patients with serious or terminal disease, who are bedbound and unstable (severe valvulopathies, post-infarction angina less than 28 days after acute myocardial infarction, severe ventricular arrhythmias in the last 6 months) or have suffered a subarachnoid haemorrhage and cardioembolic stroke as a result of valvulopathy which has already been diagnosed.

Intervention

Patient visits were conducted in accordance with a protocol which was specific for each health centre group. All the IG and CG centres followed the protocols corresponding to their group. The intervention performed at the Health Centres assigned to the IG lasted 2 years and 9 months – one visit every 4 months – and was performed by previously trained nursing personnel. To be more specific, all the personnel who had to do the fieldwork attended a training workshop at the National Health School on the secondary prevention of cardiovascular disease in general and specific aspects of the study; afterwards there was another workshop, which was exclusively for the personnel who had to perform the intervention and covered more specific intervention aspects. The intervention consisted of: information about the disease, the introduction of lifestyle changes (promotion of suitable diets, physical exercise and giving up toxic habits), individualized intervention, depending on the risk factors for each patient and the therapeutic objectives targeted for each factor, and supervision of the treatment (both prophylactic treatment and treatment targeted at risk factors) which patients received. The personnel responsible for conducting the fieldwork had a guide on the intervention and the treatments consensually agreed by the research team, in which the different components of the intervention they were to perform, which were recorded in the data collection questionnaire, were protocolized. The patients assigned to the CG were seen at the beginning and at the end of the study period.

Primary and Secondary Endpoints

Data was collected about sociodemographic variables (age, sex, marital status, occupational status and education), toxic habits, clinical history (cardiovascular diseases prior to the patient being selected as a suitable study candidate, diabetes mellitus, hypertension, dyslipidaemia, chronic obstructive pulmonary disease, renal failure and psychiatric disease), complementary tests and analytical values (glycemic levels, total cholesterol, HDL- and LDL-cholesterol and triglycerides), as well as data concerning examinations (body mass index, abdominal perimeter, systolic and diastolic blood pressure) and prescribed pharmacological treatments. The primary endpoint was the combination of total mortality and hospital cardiovascular readmissions during the study period (ischaemic cardiopathy, cardiac failure, stroke and peripheral vascular disease). This information was collected by reviewing clinical records and from interviews with patients or their relatives at each of the follow-up visits in the case of the IG and at the last visit for the CG. The secondary endpoints were: health-related quality of life measured using the generic

instrument known as the SF-36 health questionnaire, and anxiety and depression measured by means of the Goldberg Anxiety-depression Scale[13] which had been translated and validated for its use in Spain.[14]

Data collection and analysis: Case report forms were designed for the initial visit, the follow-up visits and the final visit. Both the IG and CG patients were administered the SF-36 at the initial and final visits. With the intention of minimizing losses in terms of follow-up of IG patients who failed to attend scheduled visits, the latter were contacted in order to reschedule their visit.

Calculation of sample size: assuming an estimated annual principal event rate of 5% (15% at 3 years), an absolute reduction of 5% after 3 years, an intracluster correlation coefficient of 0.01, an average of 37 patients per cluster (health centre), an alpha error of 0.05 and a statistical power of 80%, it was calculated that 42 clusters would be needed, which would mean a total of 1554 patients. Assuming losses of 15% at 3 years it was estimated that a total sample of 1787 patients would be required.

Statistical Analysis

All the analyses were performed taking into account the multicentre study design and its stratification according to autonomous communities. The baseline and results data were compared using the Chi-square test for the categorical variables, the Student *t*-test for continuous variables with a normal distribution and the Mann–Whitney test for variables which failed to show a normal distribution. Kaplan–Meier's curves were used to analyse survival and the survival curves of the study groups were compared by means of the log-rank test.

All the analyses of the efficacy of the intervention were performed by intention-to-treat analysis. All the IG patients were included in the analysis for their group, irrespective of the number of follow-up visits they attended. For the analysis of the primary variable IG patients were regarded as monitored subjects if data was available from their last or penultimate visit, in order to avoid losing patients for whom we had information during the entire follow-up period, except for the last visit. With respect to CG follow-up, subjects were contacted by telephone after 18 months of monitorization in order to verify vital data and again at the end of the study.

The data was analyzed using the STATA v 9.0 statistical program. Program routines designed for the analysis of complex samples, which enable study design, membership of clusters (health centres) and strata (autonomous communities) to be specified, and which adjust the results depending on the type of analysis, were used, variance being estimated by means of the Taylor first-order linearization technique. Statistical significance was established at levels below 5%.

RESULTS

One thousand two hundred and twenty-four patients, 624 in the IG and 600 in the CG, were recruited. Their demographic and health characteristics, which showed no statistical differences between the two groups, can be seen in Table 1.

The baseline clinical characteristics of the groups are shown in Table 2. The most common cardiovascular pathology in both groups was IC in 59.7% of cases, followed by CVA in 33.8% and PAD in 6.5%. Significant differences were not observed between the two groups with respect to their clinical characteristics.

Figure 1 shows the flow chart for the study. Twenty-three percent of the patients were lost during follow-up, without there

Table 1
Demographic and Health Characteristics of Study Groups (n = 1224)

	Intervention group (n = 624)	Control group (n = 600)
Age (years)	65.73 (64.23-67.22)	67.19 (65.95-68.43)
Sex (males) n (%)	435 (69.7)	426 (71.0)
Occupational status		
Employed	100 (16.0)	87 (14.5)
Unemployed	10 (1.6)	15 (2.5)
On sick leave or invalidity	98 (15.7)	66 (11.0)
Retired	338 (54.2)	352 (58.7)
Other	78 (12.5%)	80 (13.3)
Educational status (n = 1223)		
Illiterate	27 (4.3)	26 (4.3)
No qualifications but able to read/ write	157 (25.2)	208 (34.7)
Primary level	291 (46.7)	239 (39.8)
Secondary level	77 (12.4)	81 (13.5)
Higher educational qualification	43 (6.9)	32 (5.3)
University diploma/degree	28 (4.5)	14 (2.3)
Smoker	114 (18.3)	94 (15.7)
Drinker	42 (6.7)	42 (7.0)
Patient obese/overweight	412 (66.0)	367 (61.2)
Goldberg Scale		
Anxiety (n = 1220)	195 (31.3)	207 (34.7)
Depression (n = 1216)	280 (45.2)	277 (46.5)
Quality of Life (SF36) (n = 1204)		
Physical health	40.40 (39.55-41.25])	40.22 (38.99-41.43)
Mental health[*]	40.84 (39.77-41.91)	42.29 (41.46-43.11)

SF-36, SF-36 health questionnaire.
Data express mean (CI 95%) or n (%).
  [*] P < .05.

being any differences between the groups. The patients who were lost were not different to the patients who were followed up, either in terms of their demographic or clinical characteristics (results not shown). Amongst the lost patients, 67.1% in the IG

group were overweight/obese compared to 80.4% in the CG (P = .009).

The follow-up results are shown in Table 3. Significant differences were not found between the two groups for combined episodes of death and readmission due to cardiovascular causes (29.9% vs 25.6%). For both groups the survival curves for the principal variable, which fail to show statistically significant differences, are shown in Figure 2.

With respect to cardiovascular risk factors, the percentage of patients with well-controlled blood pressure (<140/90 mm Hg and <130/80 mm Hg in diabetics and subjects with chronic renal failure) was 52% in the IG and 51.5% in the CG (P = .88), the average glycemic level was 114 in the IG and 110 in the CG (P = .18), and the average IG LDL-c value was 103.5 and the CG equivalent was 105 (P = .59). The percentage of smokers was 8.5% in the IG and 11% in the CG (P = .07), and the mean abdominal perimeter was 100 in the IG and 102.5 in the CG (P = .07).

Significant differences were observed between the IG and the CG in terms of the percentage of patients with anxiety (20.9% vs 29.6%, P = .05) and depression (29.6% vs 41.4%, P = .02), their incidence being lower in the IG. Differences were not found in health-related quality of life between the two groups at the end of follow-up.

The treatments prescribed at baseline and at the end of the study for both groups are shown in Table 4. Significant differences were not detected for any drug, except in the use of aspirin, which increased in the IG while it decreased in the CG, and of antidepressants and anxiolytics (especially the former), which increased substantially in the IG.

DISCUSSION

In this study, which was conducted at the primary care level, we observed no differences in the main objective, which was to reduce morbidity and mortality as a result of cardiovascular diseases.

Table 2
Baseline Clinical Characteristics of Study Groups (n = 1224)

	Intervention group (n = 624)	Control group (n = 600)
Cardiovascular pathology		
Ischaemic heart disease	377 (60.4%)	354 (59.0%)
TIA or stroke	203 (32.5%)	211 (35.2%)
Peripheral vascular disease	44 (7.1%)	35 (5.8%)
Hypertension	419 (67.2%)	414 (69.0%)
Dyslipidemia	379 (60.7%)	332 (55.3%)
Diabetes	188 (30.1%)	192 (32.0%)
Previous medical history		
Ischaemic heart disease	174 (27.9%)	156 (26.0%)
Heart failure	45 (7.2%)	48 (8.0%)
Cerebrovascular accident	80 (12.8%)	71 (11.8%)
Peripheral Arterial Disease	42 (6.7%)	52 (8.7%)
COPD	48 (7.7%)	48 (8.0%)
Renal failure	21 (3.4%)	28 (4.7%)
Psychiatric disease	50 (8.0%)	56 (9.3%)
Physical examination		
Systolic blood pressure (mmHg)	133.44 (130.67-136.21)	134.58 (132.27-136.89)
Diastolic blood pressure (mmHg)	76.05 (74.67-77.43)	75.94 (74.93-76.95)
Body mass index (n = 1222)	28.72 (28.31-29.13)	28.83 (28.26-29.39)
Abdominal circumference[*] (n = 1220)	100.09 (98.93-101.26)	102.67 (100.79-104.55)
Analytical results (mg/dl)		
Baseline glucose (n = 1185)	114.59 (111.59-117.61)	116.34 (110.79-121.88)
Total cholesterol (n = 1188)	186.31 (182.14-190.48)	185.28 (181.21-189.36)
LDL-cholesterol (n = 1181)	110.42 (107.20-113.64)	112.06 (108.02-116.11)
HDL-cholesterol (n = 1180)	50.43 (47.72-53.14)	49.29 (47.16-51.43)
Triglycerides (n = 1164)	128.71 (119.55-137.87)	126.66 (119.07-134.26)

Abbreviations: COPD, chronic obstructive pulmonary disease, HDL, high-density lipoproteins, LDL, low-density lipoproteins, TIA, transient ischaemic attack.
Data express mean (CI 95%) or n (%).
  [*] P < .05.

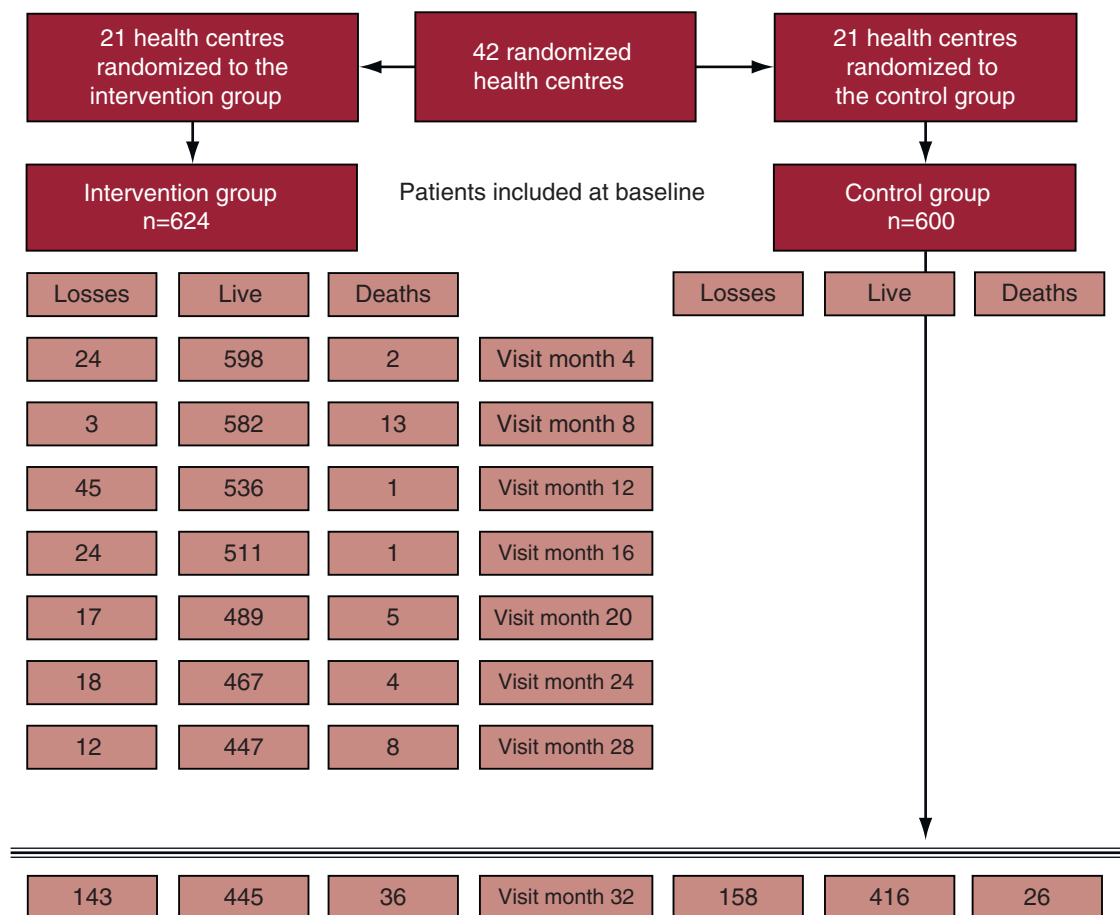| Losses	Live	Deaths		Losses	Live	Deaths
24	598	2	Visit month 4			
3	582	13	Visit month 8			
45	536	1	Visit month 12			
24	511	1	Visit month 16			
17	489	5	Visit month 20			
18	467	4	Visit month 24			
12	447	8	Visit month 28			
143	445	36	Visit month 32	158	416	26

Figure 1. Study flow chart.

Although this was a clinical trial in which health centres were randomized to avoid the possible effects of cross-contamination between individuals, in the study patients were selected from clinical practice using inclusion criteria which were not very strict and, from this viewpoint, the trial could be regarded as pragmatic. Intentionally and so as not to distance ourselves from the intrinsic infrastructure of primary care teams, the intervention was administered by personnel from the health centres themselves so that patients probably experienced the intervention as part of their routine care.

This study has various limitations which need to be mentioned. The total recruited sample was eventually smaller than we had estimated in the sample calculation, which means there might not be enough statistical power to detect statistical differences. There could also be bias in the identification of events. Although there were no significant differences in losses between one group and the other, the IG patients attended visits regularly during the study and information was collected about possible events throughout the trial. In the CG, however, patients only attended an end-of-study visit (as well as receiving a phone call halfway through the study period) after three years of follow-up, so they could more easily have forgotten whether they had been admitted to hospital. Another study limitation is that cardiovascular events could not be cross-validated against hospital data or mortality records.

The lack of efficacy of the intervention could have a number of explanations. The first might be related to the clinical characteristics of patients lost during follow-up and the fact that these patients who were lost in the CG had a worse cardiovascular risk profile. To be specific, the percentage of overweight or obese patients was higher. Amongst those who completed follow-up, 65.7% of IG patients had a history of being overweight/obese as opposed to 54.3% of the CG patients ($P < .001$). A second explanation could be linked to an awareness on the part of the control group doctors that the
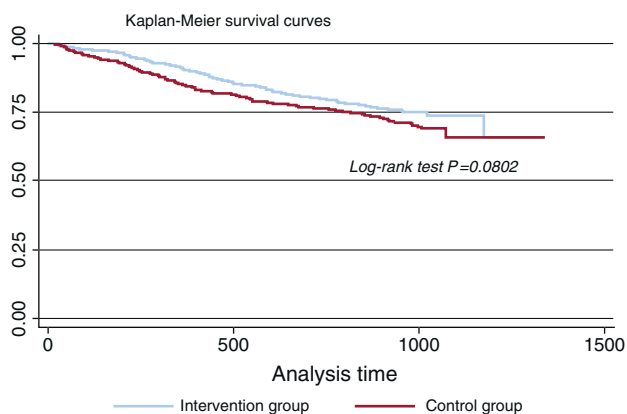

Figure 2. Survival graph for combined death and cardiovascular hospital readmission for each study group (patients who attended their final visit or died).

Table 3
Final Results Classified According to Study Group.

Patients (n = 1224)	Intervention group (n = 624)	Control group (n = 600)	P value
Follow-up			
Patients who were alive when contacted at last visit	445 (71.3)	416 (69.3)	.73
Deaths	36 (5.8)	26 (4.3)	
Total number of follow-up patients	481 (77.1)	442 (73.7)	
Losses	143 (22.9)	158 (26.3)	
Death and/or cardiovascular hospital admissions	n = 481 (77.1)	n = 442 (73.7)	.15
	144 (29.9)	113 (25.6)	
Follow up of surviving patients (n = 861; 70.3%)	445 (71.3)	416 (69.3)	
Smoker (n = 710)	31 (8.5)	38 (11.0)	.07
Physical examination			
Systolic blood pressure (mmHg) (n = 844)	132.88 (130.35-135.42)	135.31 (132.65-137.98)	.15
Diastolic blood pressure (mmHg) (n = 846)	74.93 (73.42-76.44)	74.85 (73.63-76.06)	.93
BP < 140/90 in non-diabetics	232 (52.1%) [47.0-57.2]	205 (51.5%) [45.0-58.0]	.88
BP < 130/80 in diabetics (n = 843)			
Body mass index (n = 824)	28.73 (28.22-29.24)	28.89 (28.34-29.43)	.69
Abdominal circumference (cm) (n = 833)	100.44 (98.97-101.91)	102.58 (100.96-104.21)	.07
Analytical results (mg/dl)			
Baseline glucose (n = 833)	113.99 (110.64-1187.35)	110.27 (106.70-113.83)	.18
Total cholesterol (n = 838)	177.46 (172.83-182.08)	176.98 (172.32-181.64)	.89
LDL-cholesterol (n = 816)	103.52 (98.84-108.19)	105.07 (100.82-109.33)	.59
HDL-cholesterol (n = 824)	51.22 (47.93-54.51)	49.32 (47.34-51.29)	.40
Triglycerides (n = 827)	126.43 (114.08-138.78)	130.65 (121.42-139.87)	.59
Goldberg Scale			
Anxiety (n = 753)	85 (20.9%)	103 (29.6%)	.05
Depression (n = 739)	117 (29.6%)	142 (41.4%)	.02
Quality of Life (SF36)			
Physical health (n = 777)	40.98 (40.19-41.76)	40.94 (39.95-41.92)	.95
Mental health (n = 777)	42.97 (41.90-44.04)	44.29 (43.22-45.37)	.11

Abbreviations: BP, blood pressure; HDL, high-density lipoproteins; LDL, low-density lipoproteins; SF-36, SF-36 Health Questionnaire.
Data express mean (CI 95%) or n (%).

clinical trial was being conducted, or the fact that they were more motivated with regard to cardiovascular prevention. Finally, there has been an increasing availability and implementation of guidelines in relation to the use of prophylactic drugs and the attainment of a series of therapeutic objectives. In these cases in which in routine practice intervention is fairly optimal, it is harder to find significant differences between control and intervention groups.

There are other aspects of the results which are worth highlighting. The cardiovascular risk profile at the end of the study was better in the IG than in the CG, in terms of abdominal obesity and tobacco, and prophylactic medication with anti-platelet agents and, specifically, the use of aspirin, which increases in the IG and decreases in the CG.

These aspects are clearly related to the intervention as such, given that the nursing personnel placed special emphasis on lifestyles and the importance of therapeutic compliance.

Studies which assess different strategies for improving secondary prevention results, using pragmatic randomized intervention designs at the primary care level, have been published with different results. One of these studies[15] evaluated the effect of secondary prevention units run by nursing personnel, comparing them with routine care at GP surgeries. Improvements were seen in the use of anti-platelet agents, in blood pressure and lipid control, and in the performance of physical activity and following a healthy diet. However, changes with regard to giving up smoking were not observed. The same investigators subsequently published their follow-up findings after 4 years[16] and they observed a reduction in mortality and coronary events when the two strategies were compared, although both authors comment that these results must be interpreted with caution, owing to the poor ability of the study to detect these differences and the borderline

statistical significance values (P value borderline). Neither were significant differences in cardiovascular morbidity and mortality observed in the ICAR study[9] after the implementation of an intensive programme that ensured patients were reminded to see their GP. In the SPHERE study[7], which was conducted in Northern Ireland and in which health centres were also randomized, better control of risk factors in coronary disease patients was not observed, although there was a reduction in hospital admissions.

Another interesting result, which deserves to be highlighted, is the important reduction in the percentage of patients with depression in the IG compared to the CG, which was also associated with an important increase in antidepressant treatment in the IG. It has been demonstrated that depression is a predictor for the incidence of heart disease, and, moreover, it has a negative impact on prognosis, irrespective of other risk factors.[17,18] According to the Goldberg scale, at baseline about 45% of the patients suffered from depression with no differences between the two groups, while at the end of the study 30% of the IG and 41% of the CG were depressed. As well as addressing classic risk factors and trying to meet the therapeutic targets set by guidelines, it is also important to take into account other factors which are linked to prognosis, such as depression, and to adopt the most appropriate therapeutic and non-therapeutic measures for these patients. When we analyzed the entire population (data not shown), 61% of the women and 39% of the men had been diagnosed with depression and 35% of the depressed patients suffered an event within 3 years, while 22% of the patients without depression suffered an event (P<.001). Future studies in the context of a clinical trial should explore the efficacy of detecting and treating depression and its treatment in the prognosis of patients who have suffered from cardiovascular disease.

Table 4
Standard Treatment for Study Groups

	Intervention group	Control group
Anti-platelet agents		
Baseline visit	531 (85.1)	522 (87.2)
Final visit	362 (81.4)	338 (81.5)
Aspirin		
Baseline visit	405 (64.9)	417 (69.6)
Final visit	292 (65.6)	277 (66.8)
Hypolipaemic agents		
Baseline visit	418 (66.9)	400 (66.7)
Final visit	327 (73.5)	310 (74.7)
Statins		
Baseline visit	407 (65.2)	394 (65.8)
Final visit	321 (72.1)	301 (72.5)
Beta blockers		
Baseline visit	279 (44.7)	278 (46.6)
Final visit	198 (44.5)	203 (49.2)
ACE inhibitors		
Baseline visit	239 (38.4)	242 (40.6)
Final visit	166 (37.3)	163 (39.5)
Angiotensin II antagonists		
Baseline visit	97 (15.6)	110 (18.5)
Final visit	101 (22.8)	89 (21.5)
Anticoagulants		
Baseline visit	63 (10.1)	64 (10.7)
Final visit	60 (13.5)	48 (11.6)
Antidiabetic drugs		
Baseline visit	157 (25.2)	163 (27.3)
Final visit	112 (25.2)	114 (27.5)
Diuretics		
Baseline visit	92 (14.8)	96 (16.1)
Final visit	106 (23.8)	82 (19.8)
Antidepressants		
Baseline visit	17 (2.7)	17 (2.9)
Final visit	34 (7.6)	13 (3.1)
Anxiolytics		
Baseline visit	37 (5.9)	38 (6.4)
Final visit	40 (9.0)	31 (7.5)

ACE, angiotensin converting enzyme inhibitors.
Data express n (%).

CONCLUSIONS

A comprehensive secondary prevention of cardiovascular disease programme is not effective in reducing cardiovascular morbidity and mortality, but it is able to improve some aspects which are related to healthy habits and to reduce anxiety and depression in these patients.

FUNDING

APPENDIX A

A.1. PREseAP Study Investigators

Aragón: Ariño, Dolores (Main investigator); Abancens, Mercedes; Arroyo, Virginia; Miñana, Ana; Oliván, Bárbara; Reixa, Sol y Turón, José Mª.

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