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Effect of an Educational Program (PEGASE) on Cardiovascular Risk in Hypercholesterolaemic Patients

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Abstract
Background Many studies have demonstrated a gap between guidelines for the prevention of cardiovascular disease (CVD) and their implementation in clinical practice.
Aim The PEGASE education program has been devised with an aim to improve the management of patients at high risk of CVD.
Methods In a multicentre study carried out from 2001–2004 in France, 96 participating physicians were randomized into a "trained" group, which included 398 "educated" patients, and a "non-trained" group, which included 242 "non-educated" patients. Educated patients received six hospital-based educational sessions, four collective and two individual. Framingham score, smoking, lipid levels, glycaemia, blood pressure, dietary intake and drug compliance, as well as quality of life, were evaluated at baseline (M0) and 6 months (M6). The primary endpoint of the study was the efficacy of the PEGASE program in reducing global CVD risk in high-risk patients.
Results The Framingham score was calculated for 473 patients. The Framingham score improved significantly at M6 vs M0 in the educated group (13.0±8.21 *vs* 13.6±8.48, d=−0.658, p=0.016), but not in the non-educated group (12.5±8.19 *vs* 12.4±7.81, d=+0.064, p=0.836); the mean change between the two groups did not reach significance. Quality of life, LDL-c level and diet scores improved in the "educated" group only.
Conclusions The PEGASE education program improved risk factors for CVD, although global assessment by Framingham score was not significantly different between groups. This program, aimed at meeting needs and expectations of patients and physicians, was easily implemented in all hospital centres.

Key words Educational program · Cardiovascular prevention · Cholesterol · Framingham score · PEGASE

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Introduction

Cardiovascular disease (CVD) remains a leading cause of death in the world [1]. The proportion of deaths attributable to CVD is increasing; in 2005, 17.5 million people worldwide were estimated to have died from CVD, while the projected figure for 2015 is 20.0 million [2]. In addition, the proportion of patients at high risk of a cardiovascular event in populations previously not known for high rates of CVD, such as Japanese and Indians, is also increasing [3, 4]. Thus, the prevention of CVD via the modification of cardiovascular risk factors is a worldwide concern.

The occurrence of CVD is strongly related to a limited number of potentially modifiable psychosocial and physiological factors [5]. Randomized trials have unequivocally demonstrated that intensive control of multiple risk factors by lifestyle changes and therapeutic interventions substantially reduces cardiovascular mortality and morbidity [6–8]. However, studies such as NHANES, Euroaspire [9, 10], and others [11–14] have demonstrated a gap between guidelines for CVD prevention and their actual application in clinical practice. The prevalence of modifiable risk factors was high and the use of drug therapies was inadequate to achieve blood pressure (BP) and lipid goals [14–16], due to insufficient adherence of physicians to guidelines [14], poor long-term compliance of patients with their treatment and/or lifestyle advice [17–19] and difficulty in changing risk behaviours, which have become habits over many years [20].

Hence, improvement of the management of cardiovascular risk factors requires specific intervention such as therapeutic education programs [21]. However, most patients at high risk of CVD are seen in clinical practice within the traditional model of primary care delivery, which often focuses on acute problems [22]. Lack of time, insufficient knowledge and lack of appropriate educational tools are well-known barriers to primary care physicians in providing patients' education [22, 23]. Therapeutic education is a structured, dynamic process involving practical training sessions based on a diverse set of skills and tools, provided by a multidisciplinary team. With this aim, the PEGASE program, an educational program for improved management of high CVD-risk patients, involving the combined training of physicians and education of their patients, has been implemented [24].

We conducted a randomized controlled trial to assess the efficacy of this program at reducing global CVD risk in high-risk patients (primary endpoint).

Methods

This non-blinded, randomized, multicentre controlled study was conducted according to the Declaration of Helsinki and the Huriet French law, in 6 French hospital care centres, from December 2001 to March 2004. The study protocol was approved by the ethics committee of the Pitié-Salpetrière hospital (Paris, France). Before enrolment, all participants signed an informed consent form.

Intervention: description of the PEGASE education program

The patients' education program was designed by EDU-SANTE Company (Paris). It was derived from the behavioural change model of Prochaska et al. [25], according to the education quality criteria of the World Health Organization [26]. It consisted of six educational sessions provided by an on-site physician (caregiver coordinator) and his team (one nurse and one nutritionist) from six healthcare hospital centres for CVD prevention. Its implementation included a thorough preliminary analysis of the patients' expectations in terms of education and of the physicians' difficulties in delivering their education message [27]. All caregiver coordinators, nurses and nutritionists received training for 2 days on how to use PEGASE education program.

The PEGASE education program has been detailed elsewhere [24]. Briefly, this program used easily understandable, simple methods and materials during four collective and two individual sessions and comprised three stages (increase awareness on CVD risks, start action and maintain action). At the first collective educational session, the Photolanguage® tool was used to help patients identify their own criteria for health and sickness, and which were their major threats. Then they were all invited to create a patchwork figure (using coloured cards) representing an imaginative patient with several risk factors on which they were able to project future CV risks, keeping a distance from their own emotions. During the second and third collective sessions, information about physical activity and healthy diet was given, together with the development of a positive attitude towards a healthy food pattern. This was achieved through educational pamphlets and discussion of clinical cases. Barriers to drug adherence were discussed among groups. At the last collective session, a game with questions and answers mainly focused on cholesterol management helped patients to measure their knowledge. A leaflet with core information was given at the end of each collective session. During the two individual sessions, the caregiver coordinator monitored progress and reinforced educational messages. Individual goals were translated into concrete actions related to diet, physical activity and/or better treatment adherence. Behavioural change recommendations were broken into small, achievable steps.

Investigators

Investigators, comprising primary care general practitioners, cardiologists and endocrinologists, were the usual correspondents of the six participating healthcare hospital centres. They were recruited on a voluntary basis from lists established by the centres and were managed by the caregiver coordinator located in one of the participating hospital centres.

Randomization

Investigators were randomized into two groups, one being subjected to a specific training intervention, the other forming the control group that did not receive any training. Training consisted of an attendance at a half-day workshop on cardiovascular risk factor management and how to increase patients' awareness and motivation. Randomization was performed by simple random sampling. The investigators were randomized rather than patients, to avoid "contamination" of non-educated patients by an attending physician who would initially be trained. The patients included by the "trained physicians" therefore constituted the "educated patient" group and referred to the healthcare hospital centers. The subjects included by the "non-trained physicians" formed the "non-educated patient" group.

Subjects

To be eligible for enrolment, patients had to fulfil the following criteria: aged 18 years or more, never been followed on a long-term basis by a healthcare centre specialized in patient education, and belonging to one of the three following categories:

Primary prevention:

- Category I: Patients with LDL-cholesterol (LDL-c) levels >220 mg/dL (5.7 mmol/L) before treatment;
- Category II: Patients with LDL-c levels >160 mg/dL (4.1 mmol/L) and <220 mg/dL (5.7 mmol/L) before treatment with at least one of the following cardiovascular risk factors: high BP (BP>140/90 and/or antihypertensive treatment), obesity (BMI≥30 kg/m^2), diabetes (fasting glycaemia≥126 mg/dL and/or antidiabetic treatment), current smoking, familial history of CVD or HDL-cholesterol (HDL-c)<35 mg/dL (0.9 mmol/L).

Secondary prevention:

- Category III: Patients suffering from coronary disease and having an LDL-c level>130 mg/dL (3.4 mmol/L) before treatment. If the patient was receiving a lipid-lowering therapy, lipid levels before treatment initiation were taken into account.

Patients with language problems and/or with difficulty understanding French, pregnant women or nursing mothers were excluded.

Study design

The primary endpoint of the study was the efficacy of the PEGASE program in reducing global CVD risk. Patients were screened by their primary care physician. Each primary care investigator had to include the first six patients meeting all inclusion/exclusion criteria. Both educated and non-educated groups were followed for 6 months. Participants in both groups attended two visits within the 6-month study period and received standard care from their primary physician. In addition, the patients from the educated group were referred to receive the special education sessions during the 6-month period (PEGASE education program) at the centre closest to their residence.

All patients underwent the following: at inclusion (M0), the primary care investigator filled in a medical questionnaire, and at M0 and M6 recorded medical data including BP, biological profile and smoking evaluation. The interpretation of the information collected during consultations was left to the discretion of the primary physicians in the non-educated patient group. Physicians in this group were not given any additional information or training to allow them to interpret the data.

All patients received a prescription for laboratory tests and four auto-questionnaires evaluating quality of life (SF-36) [28], pharmacological compliance, physical activity [29] and dietary intake [30].

BP measurement

BP was always taken using the same arm, with the same measuring apparatus. The first measure was taken for the first time after 5 min at rest, then twice more with a 2 min-interval. The recorded value was the mean of the last two measures.

Smoking status

At each visit patients were asked how many cigarettes they smoke per day and for how many years.

All the questionnaires filled in by the patients and physicians were sent back for monitoring and data processing to the company in charge of the database analysis.

Primary outcome

The efficacy of the education program was assessed by measurement of the global CVD risk defined by the

modified Framingham Score (Framingham-Anderson model) [31], adapted by Laurier for application to the French population [32]. It is calculated by evaluating smoking and diabetes, BP, HDL-c and total cholesterol (TC) levels. It estimates the risk of CVD incidence over the next 10 years and can be stratified into three categories: <10%—low risk; 10–20%—intermediate risk; and >20%—high risk.

Secondary outcomes

Secondary criteria were dietary and drug compliance, evolution of physical activity, quality of life, smoking, LDL-c and triglyceride levels, glycaemia and BP.

Laboratory tests for biological parameters

All the laboratory analysis for measurement of TC, LDL-c, HDL-c, triglycerides and fasting glycaemia were centralized in one laboratory (LCL Laboratory, Paris), at M0 and M6. LDL-c was directly measured by an enzymatic colorimetric test in homogenized phase (Roche diagnostics).

Dietary compliance

Dietary compliance was assessed by the measure of a "cardio-protective" diet score, ranging from −22 to +29. This score was calculated from a dietary questionnaire which recorded saturated, mono-unsaturated, and poly-unsaturated $n-3$ and $n-6$ fatty acid intake as well as fruit, vegetable and wine intake [29].

Physical activity questionnaire

This questionnaire was adapted from the validated English questionnaire of Norman et al. [29]. The frequency of performing five activities (professional activity, walking/cycling, housework, TV/reading, physical activities) was evaluated and the number of sleeping hours was recorded with a recall period of 3 months. The score varied from 5 to 27, the lowest score corresponding to very low activity.

Lipid-lowering drug compliance

For each drug, the theoretical number of doses to be taken daily was multiplied by 7, to obtain a theoretical number of doses per week.

To evaluate compliance, the patient calculated the sum of doses taken during the previous week. The drug compliance was then calculated by dividing the sum of doses per week by the theoretical doses number per week, and expressed as a percentage.

Quality of life

Scores obtained from the SF-36 questionnaire [28] were described for patients having a questionnaire with <50% of missing data at M0 or M6. For those presenting a questionnaire with <50% of missing data at both visits, quality of life evolution from M0 to M6 was also described.

Statistical analyses

In the absence of reference data about the target population, and with the assumption that to detect a mean difference of 10% in the total CVD risk score between educated and non-educated groups at 6 months, a sample size of 268 subjects was required in each group to achieve 90% power at an alpha risk of 0.05. Taking into account the high risk of patients' withdrawing and being lost for follow-up (33%), it was necessary to include 360 patients in each group, i.e. a total of 720 subjects to have 600 evaluable patients.

Statistical analysis was performed with SPSS version 11.5 for Windows® software. Quantitative parameters were expressed by number of patients, mean, standard deviation, and qualitative parameters by number and percentage of patients.

Between educated and non-educated groups comparisons were assessed using variance analysis for quantitative criteria and Chi^2 test for qualitative criteria. Within each group from M0 to M6 (6 month follow-up period), time-effect analyses were performed by Student's paired t-test for quantitative variables and Mac Nemar's test for qualitative variables. All statistical tests were performed using a statistical significance threshold of 0.05.

Results

Participants flow and baseline characteristics

Participants' flow chart is presented in Fig. 1. During the inclusion period, from November 2001 to end of March 2003, 96 primary care physicians enrolled 640 patients. It appears that the dropout rate was slightly higher for educated patients than for non-educated (15.5% versus 11%) but there was no clear reason to explain this difference.

Analysis for the primary outcome was performed for the 473 patients for whom a Framingham score could be calculated at both M0 and M6. Demographic characteristics at baseline were similar between educated and non-educated groups, and there was no statistical difference between the groups with regard to risk factor distribution (Table 1).

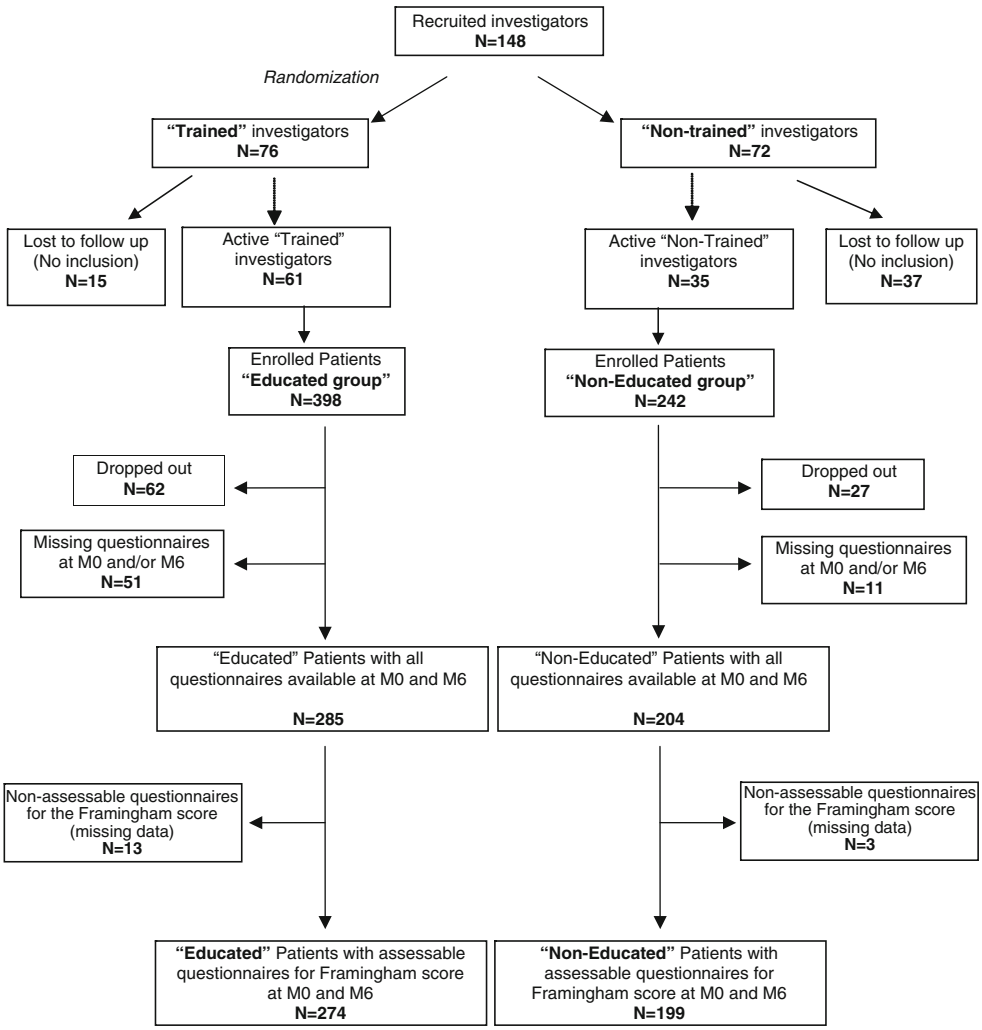

Fig. 1 Flow chart of the participants included in the PEGASE study

At baseline, 77% of patients were in a primary prevention category (I or II), whereas 23% were in category III (Table 1). Mean LDL-c levels at inclusion in patients belonging to category I, II and III were 155, 142 and 119 mg/dL, respectively. Mean TC/HDL-c ratios were 4.75, 4.41 and 4.26, respectively.

Primary outcome

In the intervention/educated group, the mean Framingham score decreased significantly between M0 and M6 (difference: −0.658, $p=0.016$) whereas in the non-educated group, the mean score did not change over the study period (difference: +0.064, $p=0.836$). However, the mean change between the two groups did not reach statistical significance ($p=0.08$). At M0 and M6, the mean Framingham score was not significantly different between the educated and non-educated groups (13.6±8.48 versus 12.4±7.81, $p=0.121$ and 13.0±8.21 versus 12.5±8.19, $p=0.542$ respectively).

Secondary outcomes

A significant difference between educated and non-educated groups was observed for LDL-c (+8.0 mg/dL; $t=2.16$, $p=0.032$), with no significant change over time in the intervention group compared with a significant increase in the control group (+2.0 mg/dL, $p=0.452$ versus +10.0 mg/dL, $p<10^{-3}$).

TC, drug compliance and cardio-protective diet score were significantly improved from M0 to M6 in the educated group, whereas they did not change in the control group (Table 2). In contrast, the number of patients with moderate to severe hypertension increased significantly by 10.2% ($p=0.011$) over time in the non-educated group only. Total cholesterol/HDL-c ratio did not vary significantly from M0 to M6 either in the educated group (4.57±1.4 to 4.45±2.17, $p=0.12$) or in the non-educated group (4.24±1.32 to 4.18±1.47, $p=0.4$). The additional criteria (fasting glycaemia, triglycerides, physical activity score, HDL-c, systolic BP, smoking) were not significantly modified in either group.

Table 1 Socio-demographic and clinical characteristics of patients at baseline

Characteristics		Educated (*N*=274)	Non-educated (*N*=199)	*p* value
Sex *n* (%)	Male	167 (60.9)	117 (58.8)	0.704
	Female	107 (39.1)	82 (41.2)	
Age (years)	Mean+/−SD	56.9±10.1	58.1±12.0	0.059
Marital status, *n* (%)	Married	187 (69.3)	139 (70.2)	0.067
	Cohabitation	18 (6.7)	22 (11.1)	
	Single	23 (8.5)	8 (4.0)	
	Widow	15 (5.6)	16 (8.1)	
	Separated	27 (10.0)	13 (6.6)	
Education, *n* (%)	No education	20 (7.8)	25 (12.6)	0.446
	Technical school	133 (52.0)	97 (48.7)	
	Secondary education	37 (14.5)	27 (13.6)	
	Higher education	66 (25.8)	50 (25.1)	
Professional situation, *n* (%)	Working	116 (42.5)	83 (42.1)	0.549
	Training	– (–)	1 (0.5)	
	Retired	132 (48.4)	90 (45.7)	
	Non-working	18 (6.6)	19 (9.6)	
	Unemployed	7 (2.6)	4 (2.0)	
Geographical environment, *n* (%)	Countryside	66 (24.4)	56 (28.1)	0.395
	Urban environment	204 (75.6)	143 (71.9)	
Primary prevention				
Cat. I: LDL-c>2.2 g/L		42 (15.3)	32 (16.1)	NS
Cat. II: 1.6 g/L<LDL-c<2.2 g/L		161 (58.8)	129 (64.8)	NS
+HBP (BP>140/90 or treatment)		85 (31.0)	76 (38.2)	NS
+Obesity (BMI≥30)		58 (21.2)	36 (18.1)	NS
+Diabetes (FGlc≥1.26 g/L or treatment)		20 (7.3)	21 (10.6)	NS
+Smoking		52 (19.0)	47 (23.6)	NS
+CVD familial history		58 (21.2)	41 (20.6)	NS
+HDL-C<0.35 g/L		7 (2.6)	12 (6.0)	NS
Secondary prevention (Cat. III)		71 (25.9)	38 (19.1)	NS

FGlc fasting glycemia, *HBP* high blood pressure

Quality of life (Table 3) was significantly improved after intervention in the educated group, with a significant difference between the mean change of the physical component score of the educated group and the non-educated group (+2.57, p=0.001 vs −0.5, p=0.356), as well as for several other characteristics (physical functioning, role-physical, general health and vitality). There was no significant difference in mental component score between the two groups.

Analysis according to patients' tertiles

An analysis of Framingham score reduction according to patients' tertiles within the educated group was performed. The objective was to analyze which patients would benefit most from the PEGASE program. The best responders, i.e. patients with a decrease in Framingham score of more than 1.9 points between M0 and M6, were compared with the other patients.

The baseline clinical characteristics of the "best responders" were significantly different from those of the other patients, with a higher Framingham score and a higher level of all major risk factors except for smoking (Table 4). There were more diabetic, and hypertensive patients but fewer smokers among the best responders than others (8.6% vs 24.3%, p=0.002). They were of the same socio-economic background, with similar levels of education and lifestyle compared with the other patients.

Discussion

Our study demonstrated that the PEGASE education program has an effect on quality of life, dietary intake and LDL-c level of patients at high risk of CVD, after 6 months of intervention. However, this did not result in a significant change in the global CVD risk score between intervention and control groups.

Regarding the primary outcome in the PEGASE study, i.e. the Framingham score, this was a particularly difficult endpoint for an education program evaluation [33–36]. As our objective was to implement the PEGASE program in other centres, it was necessary to use strong validated criteria. We have chosen to use the Framingham score to

Table 2 Delta changes in secondary criteria in educated and non-educated groups from M0 to M6

Characteristics	Educated (n=274)		Non-educated (n=199)	
	Change from baseline	p-value (M6 vs M0)[a]	Change from baseline	p-value (M6 vs M0)[a]
Framingham score parameters				
Total cholesterol (g/L)	−0.0764	0.0006	−0.034	0.246
HDL-c (g/L)	+0.0087	0.27	+0.0038	0.70
SBP (mmHg)	−0.63	0.494	+0.34	0.733
Smoking	−13.7%	0.065	−12.7%	0.146
Auto-evaluated criteria				
Total "cardio-protective diet" Score (from −22 to +29)[b]	+4.0	$<10^{-3}$	+0.0174	0.969
Physical activity score (from 5 to 27)[c]	+0.214	0.190	−0.03	0.842
Drug compliance score (lipid lowering drugs) (0–100%)[d]	+8.84	0.032	+0.52	0.874

SBP systolic blood pressure, *HDL-c* high density lipoprotein
[a] Between-group analysis, p: NS
[b] Educated/non-educated n=87/86
[c] Educated/non-educated n=182/176
[d] Educated/non-educated n=92/83

display potential small modifications of the major risk factors that would not be significant if they were taken independently. The slight improvement of the Framingham score in this population in the educated group from baseline to 6 months could thus be due to improvements in TC and to a moderate improvement of each parameter contributing to the global score.

The improvement observed in LDL-c levels in the educated group may be the consequence of better drug compliance and a healthier diet, significantly improved by the PEGASE program. The improvement of the diet quality was mainly due to a greater consumption of fruit and vegetables by the educated patients (data not shown), which is known to be associated with a lower risk of CVD [37]. These results show that the education program was particularly efficient in changing patients' habits towards a more "cardioprotective" diet. The use of simple tools in the program allowed enhancement of patients' global motivation, which was essential for the success of the intervention.

Several randomized controlled trials have been conducted to evaluate multimodal intervention using counselling and education with or without pharmacological treatments in patients at high risk of CVD [38–44]; generally, these programs were found to have a favourable impact on CVD risk factors and related mortality. However, the type of educational intervention was seldom reported and many educational programs consisted of simple information passively received by the patient in forms of leaflets, videos, postal reminders, telephone calls or advices dispensed by health care providers [40, 45–49]. In contrast, the PEGASE program is a real therapeutic education program, in which patients had to play an active role by identifying their own health status and risk criteria with the help of the Photolanguage® method [50, 51], analyzing

Table 3 Changes in quality of life scores of educated versus non-educated patients from M0 to M6

SF-36 scales	Educated (n=221)		Non-educated (n=188)	
	Change from baseline	p-value (M6 vs M0)[a]	Change from baseline	p-value (M6 vs M0)[a]
Physical functioning	+6.72	10^{-3}	−0.63	0.556
Role-physical	+7.91	0.002	+1.08	0.656
Body pain	+2.76	0.09	−0.95	0.567
General health	+2.81	0.005	−0.64	0.579
Vitality	+3.43	0.002	−1.47	0.222
Social functioning	+2.09	0.196	+0.73	0.622
Role-emotional	+2.22	0.401	+3.55	0.158
Mental health	+1.79	0.12	+0.13	0.909
Mental component score	+0.53	0.457	+0.69	0.307
Physical component score	+2.57	10^{-3}	−0.5	0.356

[a] Between group analysis, p=NS

Table 4 Baseline characteristics of patients whose Framingham score mostly decreased from M0 to M6 compared to others

Characteristics at M0	Best respondent patients (N=93)	Other patients (N=181)	Mean±SD	Mean±SD	p value
	n (%)	n (%)			
Primary prevention Cat I	13 (14.0)	29 (16.0)			NS
Primary prevention Cat II	60 (64.5)	101 (55.8)			NS
+Hypertension (BP>140/90 or treatment)	36 (38.7)	49 (27.1)			0.049
+Diabetes (FGlc≥1.26 g/L or treatment)	11 (11.8)	9 (5.0)			0.039
+Current smoking	8 (8.6)	44 (24.3)			0.002
Secondary prevention Cat III	20 (21.5)	51 (28.2)			NS
Framingham score			18.3±7.5	11.2±7.9	$<10^{-3}$
Age (years)			59.5±8.9	55.6±10.5	0.002
SBP (mmHg)			140.6±15.0	128.23±12.4	$<10^{-3}$
DBP (mmHg)			82.3±8.7	76.6±8.9	$<10^{-3}$
Fasting glycemia (g/L)			1.13±0.27	1.01±0.21	$<10^{-3}$
Total cholesterol (g/L)			2.40±0.52	2.20±0.51	0.003
HDL (g/L)			0.50±0.12	0.54±0.18	0.034
LDL-c (g/L)			1.57±0.44	1.38±0.42	0.001

FGlc fasting glycemia

their lifestyle behaviour and providing a personal plan for the improvement of one or several risk factors. Whether there is a significant difference between passive and active *programs remains* to be determined, since the results of existing studies are somewhat mixed; some active interventions resulted in no differences between groups [39], while some passive programs did show an increase in compliance with telephone based interventions [48]. However, contrary to other cardiovascular management programs [43, 44], the PEGASE program is applicable to all categories of patients at risk for CVD whether in primary or secondary prevention, making it more broadly applicable to the general CVD patient population.

PEGASE program has been shown to be more efficient in patients at the highest risk for CVD, a result consistent with those observed in other clinical trials: people at highest risk for CVD benefit most either from hypertension control or from cholesterol lowering interventions [38, 52]. However, good responders to PEGASE program smoked less frequently than other patients and smoking as a risk factor may be more difficult to modify than other conditions due to the addiction that tobacco induces. Evidence suggests that intensive smoking cessation programs (combinations of intensive counselling and follow-up with or without pharmacological intervention) can significantly increase both short- and long-term quit rates compared with minimal or no intervention [53–55]. Many patients believe that they can successfully quit smoking on their own, despite many having tried and failed in the past; [56] thus, patients need to be educated regarding the fact that smoking cessation programs can significantly increase their chances of long-term success.

There are several limitations to our study. The present study did not have sufficient power and/or period of follow-up to achieve a significant difference between the two study groups. Extension of the study may have revealed this significance, since the score improvement was already substantial after only 6 months of intervention. As shown in other studies [24, 57, 58], the benefits in terms of cardiovascular event reduction may occur over time and not in the early stages of an intervention program. Furthermore, behavioural changes require a long "step by step" process [20, 24]. The lack of significance in this study could also be explained by the lower number of evaluated patients at 6 months compared to that estimated in the study protocol, or by an underestimation of the initial CVD risk level taken for the primary hypothesis. As expected in this kind of open study evaluating an education program, the number of patients and physicians who dropped out was important. However, the withdrawal rate in the present study was 11% for the non-educated group and 15.5% for the educated group; this rate is similar to that of other studies [37, 56].

Another reason for the lack of significance could be the secondary motivation of both physicians and patients in the "non-educated" group, related to their participation in an educational program. Instead of a potential increase in this group, the global risk score did not change significantly. Knowing that their risk factors were going to be carefully monitored, both patients and physicians of the "non-educated" group may have been motivated to control these risk factors to a greater extent than normal; this phenomenon has been described in other studies [47]. Smoking, which decreased by the same extent (about 13%) in both groups, clearly showed that the non-educated group had also

made efforts to improve its habits. Finally, education strategies might be less effective in diseases such as hypercholesterolemia, which is usually perceived as a non-severe condition, than for other symptomatic diseases such as diabetes mellitus, which is recognized as a major risk factor.

In conclusion, we observed a significant improvement in the Framingham score in the educated group while there was no change in the non-educated group. However, the difference between groups did not reach statistical significance. This result might be explained by the attrition rate, resulting in only 473 evaluable patients instead of the 600 planned. Furthermore, most educational programs tend to evaluate the benefit on softer endpoints.

Obviously, more research is needed to find out the most effective strategy to use for hypercholesterolemic patients at risk for CVD. More specifically, there is a need to assess whether a specific approach (focused on a single risk factor such as hypercholesterolemia or a single behaviour such as dietary habit for example) leads to greater improvement in cardiovascular risk than a more global approach in which messages can be diluted or less well understood. Further research should probably focus on patients at the highest risk and with a low level of information. Indeed, conducting a trial which implies signed consent and rather strict rules is often associated with a selection bias towards the more motivated and educated patients.

The present study showed that a simple and well-conceived education program could have an impact on LDL-c levels, patients' health perception, quality of life and dietary intake via positive changes in the health care provider–patient dynamic. This study was carried out in real-life practice conditions, i.e. the physicians could adjust the treatments at their discretion and the patients could eat what they wanted as long as they followed the dietary advice. Supported by patients and physicians, the PEGASE program could thus easily be implemented and generalized in other centres.

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