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EFFECT OF AN EDUCATIONAL PROGRAM IN PRIMARY CARE: THE CASE OF LIPID CONTROL IN CARDIO-CEREBROVASCULAR PREVENTION

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Lowering blood cholesterol levels reduces the risk of coronary heart disease. However, the effect of interventions depends on the patients' adherence to treatment. Primary care plays an important role in the detection, treatment and monitoring of disease, therefore different educational programs (EP) have been implemented to improve disease management in general practice. The present study is aimed to assess whether a general practitioner auditing and feedback EP may improve dyslipidaemia management in a primary care setting and to evaluate patients' adherence to prescribed lipid-lowering treatment. The quality of cardiovascular and cerebrovascular disease prevention before and after the implementation of an EP offered to 25 general practitioners (GPs), was evaluated. Clinical and prescription data on patients receiving at least one lipid-lowering treatment was collected. To evaluate the quality of the healthcare service provided, clinical and biochemical outcomes, and drug-utilization, process indicators were set up. Adherence was evaluated before and after the EP as the "Medication Possession Ratio" (MPR). A correlation analysis was carried out to estimate the effect of the MPR in achieving pre-defined clinical end-points. Prescription data for lipid-lowering drugs was collected in a sample of 839 patients. While no differences in the achievement of blood lipid targets were observed, a slight but significant improvement of the MPR was registered after the EP (MPR >0.8=64.2% *vs* 60.6%, p=0.0426). Moreover, high levels of statin adherence were associated with the achievement of total blood cholesterol target (OR=3.3 for MPR >0.8 *vs* MPR <0.5, 95% CI:1.7-6.7) or LDL therapeutic goal (OR=3.3 for MPR >0.8 *vs* MPR <0.5, 95% CI:1.5-7.2). The EP partially improved the defined clinical targets; probably, a more patient-based approach could be more appropriate to achieve the defined target. Further studies are needed to identify how healthcare services can be improved.

Cardio-cerebrovascular (CCV) diseases have a major impact on patient morbidity and mortality, and are associated with significant costs to healthcare budgets worldwide. CCV diseases are the most

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common cause of death in Italy, with an incidence of 2.80 and 1.84 events per 1,000 inhabitants, for men and women, respectively (1).

Hypercholesterolemia is one of the most relevant risk factors for the development of atherosclerosis and, as a consequence, for ischemic disease (2, 3). Lipid-lowering drugs, and statins in particular, have been demonstrated to reduce the risk of death and CCV disease in different cohorts of patients (4-7). However, the effect of pharmacological and non-pharmacological interventions depends on the patients' adherence to prescriptions and recommendations. Several studies showed a rather low rate of statin prescribing and a lack of adherence to treatment in clinical practice (8-11), leading to lower clinical benefits compared to patients with ideal compliance rates.

Primary care plays an important role in the detection, treatment and monitoring of patients with high risk of developing CCV disease both in primary and secondary prevention. Therefore, many European countries have implemented large-scale programs to improve prevention and risk management of CCV diseases in primary care (12). The European group for prevention and risk management in primary care has developed several possible strategies to improve the effective management of CCV diseases in primary care including the development of assessment and feedback instruments to measure the quality of healthcare service in general practice and the identification and implementation of best practices according to different organizational contexts.

Auditing and feedback are commonly used to improve the quality of healthcare in a range of evidence-based activities. The auditing cycle emphasizes the need to establish the best practice, to set standards, to then measure practice versus standards, and then to change practice in order to reach those standards. However, the benefits of auditing on actual practice effectiveness are uncertain. Jamtvedt et al., in their systematic review in the Cochrane Database (13), concluded that "Audit and feedback can be effective in improving professional practice. When it is effective, the effects are generally small to moderate. The absolute effects of audit and feedback are more likely to be larger when baseline adherence to recommended practice is low".

Even though the information obtained using the data warehousing approach is useful to evaluate the real pattern of prescriptions in clinical practice, there is a lack of information on the true effectiveness of an intervention in improving healthcare (14).

Several studies conducted using the Arianna general practice database (15-17) underline the importance of adherence to statin therapy in improving blood lipid levels and the efficacy of training programs in achieving satisfactory results in statin users.

General practice databases are useful in obtaining information about clinical practice but little is known about the effectiveness of training programs in improving healthcare service for patients with chronic diseases. The present study therefore aims to compare the quality of cardio-cerebrovascular prevention before and after the implementation of an educational program offered to GPs by: i) measuring current patients' adherence to prescribed lipid-lowering treatment in a primary care setting of Southern Italy; ii) evaluating the associated achievement of pre-defined therapeutic goals and modification of risk factors; iii) evaluating whether a GP education program on recent developments and strategies for blood lipid control could favour the improvement of such goals in the primary care setting.

MATERIALS AND METHODS

Twenty-five GPs who provide primary care at the Local Health Unit of Caserta (Italy) and whose practice actively contributes data to the Arianna Database were offered an educational program related to cardio-cerebrovascular prevention. The ensuing study was composed of two different phases. In phase I, patients' electronic health records were retrospectively collected before the educational program was launched. The same patients' records were prospectively collected after the implementation of the program in order to investigate potential differences between the two phases. The total follow-up period was 36 months: 18 months before the educational program, which was initiated on 25thNovember 2006, and 18 months after the program. The overall observation period was from 1stJune 2005 to 31stMay 31 2008. Fig. 1 illustrates the flow of the study.

Patient inclusion and exclusion criteria

The eligible sample for this study was composed of all patients in the care of the 25 GPs participating in the

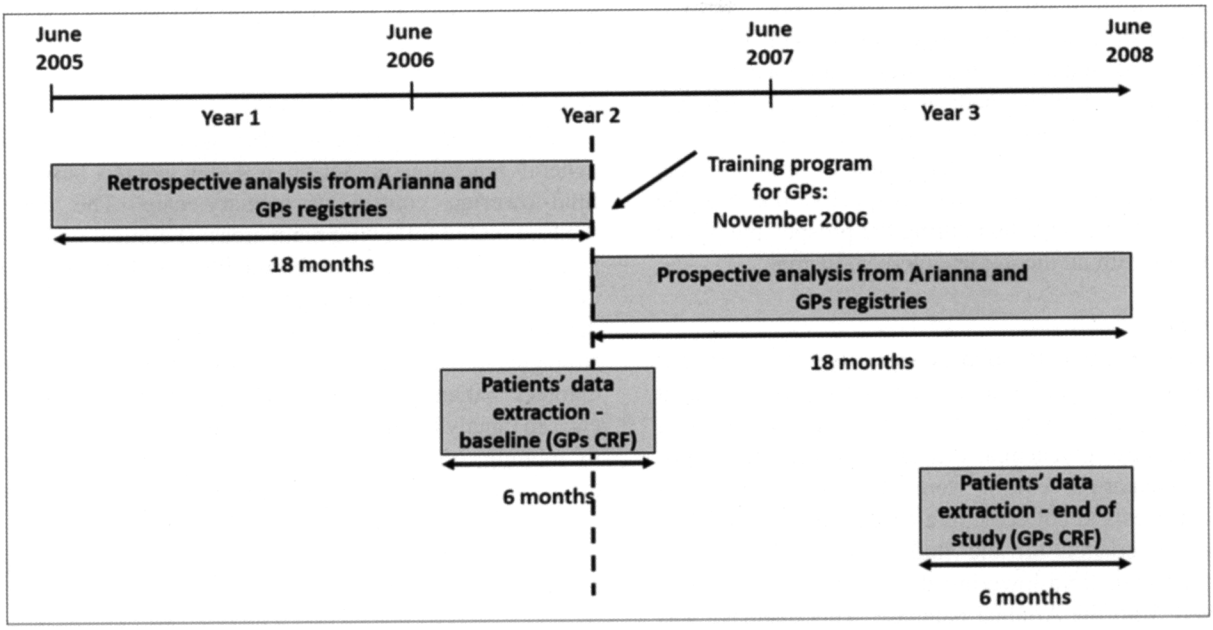

Fig. 1. *Study methodology and follow-up period.*

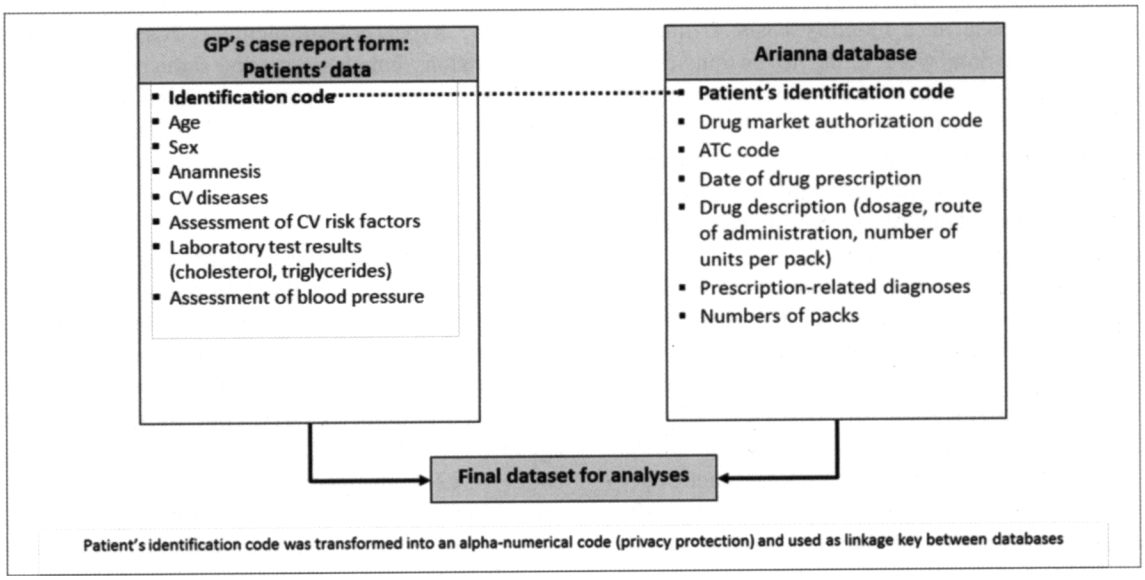

Fig. 2. *Description of data sources and database linkage.*

study, who: i) were aged ≥ 18 years at the time of the training program (considered the index date, t_0); ii) were included in the Local Health Unit list of National Health Service (NHS) beneficiaries during the entire study period; iii) were receiving at least one lipid-lowering treatment HMG CoA reductase inhibitors (ATC code: C10AA); fibrates (ATC code: C10AB); bile acid sequestrants (ATC code: C10AC); nicotinic acid and derivatives (ATC code: C10AD); other lipid-modifying agents (ATC code: C10AX); HMG CoA reductase inhibitors in combination

with other lipid-modifying agents (ATC code: C10BA) before the start date of the study; iv) gave their informed consent to participate at the study. Additionally, only patients with complete medical records were included. The following patients were excluded from the final analysis: i) patients who discontinued lipid-lowering therapy at the beginning of the prospective phase of the study; ii) patients who died during the prospective phase; iii) patients with an incomplete medical history.

Data source

Two different data sources were used to carry out this study. The demographic, anthropometric, medical history and other clinical information (i.e. lipid profile, blood pressure, glycaemia, therapy received for cardio-cerebrovascular prevention) were retrieved from personal GPs registries and collected in a case report form (CRF), specifically created for the study. This data was then integrated with lipid-lowering drug prescription records extracted from the Arianna database. This database was set up by the Caserta Local Health Agency in 2000 and currently contains information on a population of almost 400,000 inhabitants who are registered with almost 300 GPs. Participating GPs record data during their routine clinical practice using dedicated software and send complete and anonymous clinical data of their patients to the Arianna Database on a monthly basis. If quality and completeness of data were found to be outside of the defined acceptable ranges, they were investigated and back-submitted to each participating GP to receive immediate feedback. GPs failing to meet standard quality criteria were excluded from the epidemiologic surveys according to the basic standards in the management of pharmacoepidemiological investigations.

Information collected included patient demographics, drug prescriptions coded according to the Anatomical Therapeutic Chemical classification system (ATC) and their indications for use, coded by the ninth edition of International Classification of Diseases, Clinical Modification (ICD-9). Each patient's medical history was collected in a complete manner by the general practitioner irrespective of whether treatment was initiated by GPs or by specialists working in the public or private sector. In fact, in Italy outpatients receive medicines free of charge only through GP prescriptions and GPs function as gatekeepers of the National Health Service. To date, the Arianna database has been shown to provide accurate and reliable information for pharmacoepidemiological research and educational programs, as documented elsewhere (15-23).

As both the Arianna Database and CRF contain the same patient identification codes, data integration was carried out using a deterministic database linkage. The list of fields included in the data of the two sources is shown in Fig. 2.

Training program: main contents

The research group, together with a committee of general practitioners, set-up a 1-day course based on lipid-lowering control in primary care. The course focused on the following main areas: i) clinical update of main recommendations and guidelines on lipid-lowering in cardio-cerebrovascular prevention; ii) specialist-led discussions of different clinical cases (lipid-lowering strategies in patients with genetic dyslipidemic disorders, diabetes patients, secondary CCV prevention patients, etc.) iii) analysis of the informative strategies and tools to monitor efficacy, safety and use of lipid-lowering drugs. All the sections of the educational program were interactive, with general practitioners being involved in "question and answer" debates and in ad-hoc final tests to assess the physicians' knowledge.

Evaluation of patients' characteristics

During the period July 2006 – January 2007, GPs participating in the study provided baseline patient data in the case report form. Information included: i) patients' ages and sex; ii) patients' levels of education and marital status; iii) patients' medical histories (ascertained history of CCV disease, hypercholesterolemia, hypertriglyceridemia, hypertension, diabetes, smoking status and family history of CCV diseases); iv) patients' clinical data (body mass index, total, high-density and low-density cholesterol, triglycerides, systolic and diastolic blood pressure).

Drug utilization data

Patients' prescriptions were retrieved from the Arianna database over the follow-up period, including retrospective and prospective phases of the study. Patients receiving lipid-lowering drugs were also characterized according to the usage of the following medications: i) drugs used in diabetes (ATC code: A10); antithrombotic agents (ATC code: B01); drugs used in hypertension [ATC codes: C02 (anti-hypertensives), C03 (diuretics), C07 (beta-blocking agents), C08 (calcium channel blockers), C09 (agents acting on the renin-angiotensin system)].

Adherence was measured using medication possession ratio (MPR) for patients receiving treatment with HMG CoA reductase inhibitors (statins). The MPR indicates the percentage of pharmacological coverage during the follow-up (FU) period. To calculate MPR, the total number of defined daily doses (DDD) was divided by the duration of the follow-up period. Patients were classified into four different groups according to their level of adherence: i) MPR<25%; ii) 25%≤MPR<50%; iii) 50%≤MPR<80%; iv) MPR≥80%.

Evaluation of the effect of a training program on the quality of healthcare service: comparison before and after training

At the end of the study, data from the two different phases were compared to each other to evaluate whether the implementation of a training program resulted in an improvement in healthcare outcomes and services. Three different types of indicators were developed to evaluate the quality of healthcare service: i) outcome indicators; ii) drug-utilization indicators; iii) process indicators.

The first category, outcome indicators, included pre-defined clinical parameters indicating the achievement of a clinical target. Achievement of total cholesterol targets (<200 mg/dl), low-density cholesterol targets (LDL<130 mg/dl), high-density cholesterol targets (HDL≥40 mg/dl) and triglyceride targets (<200 mg/dl) were used as benchmarks, as reported by the National Cholesterol Education Program (NCEP), Adult Treatment Panel III (ATP III) guidelines (24). Moreover, patients were categorised according to their blood pressure (BP), using the European Society of Hypertension (ESH) classification (25) (optimal BP: systolic <120 mmHg and diastolic <80 mmHg; target BP: 120 mmHg≤systolic<140 mmHg and 80 mmHg≤diastolic<90 mmHg; grade I hypertension: 140 mmHg≤systolic<160 mmHg and 90 mmHg≤diastolic<100 mmHg; grade II hypertension: 160 mmHg≤systolic<180 mmHg and 100 mmHg ≤diastolic<110 mmHg; grade III hypertension: systolic ≥180 mmHg and diastolic ≥110 mmHg).

The second category, drug-utilization indicators, included parameters indicating patients' adherence to the prescribed statin regimen. The number of patients receiving statin treatment and their MPR levels in the phase before and after the GP education programme were compared

A correlation analysis was carried out to estimate the effect of the MPR on the achievement of optimal clinical targets.

The third category of indicators were process indicators. These consisted of a quantification of recorded parameters crucial to the monitoring of patients at high risk of CCV disease. A comparison between the period preceding and that following the educational program was carried out using the following indicators: i) percentage of patients with at least one cholesterol (total, LDL, HDL) assessment ii) percentage of patients with at least one body mass index (BMI) assessment; iii) percentage of patients for whom smoking status was registered; iv) percentage of patients with at least one blood pressure measurement; v) percentage of patients with at least one blood glucose test.

Statistical analysis

Statistical methods used for patients' assessment at baseline (t_0) were purely descriptive. Absolute and relative frequencies were used for categorical variables, while means and standard deviations (SDs) were used to estimate continuous variables. Univariate non-parametric tests (*chi*-square tests) were used to test potential differences between distributions before and after the educational intervention. Values were considered statistically significant if p values were lower than 0.05. Finally, a univariate logistic regression was used to estimate the association between statin adherence, as calculated by the MPR, and the achievement of target cholesterol values (total, LDL, HDL). The results of the logistic regression are reported as odds ratios (ORs) along with their 95% confidence intervals (95% CI).

Ethical considerations

In order to ensure the patients' privacy, identification codes used in both the data sources (Arianna database and GPs case report forms) were anonymised through conversion into alpha-numeric codes. The Ethics Committee of Caserta LHU approved the study. Patients included in the study had to give their informed consent to permit the use of their data.

RESULTS

Patients' characteristics

The study sample consisted of 877 eligible subjects. The patients' characteristics are summarized in Table I. There was a slightly higher number of men (55.1%, mean age=64.7 yrs; SD=10.1) compared to women (44.9%, mean age=67.7 yrs; SD=9.4). About 73% of patients (n=642) were classified as eligible for secondary prevention (i.e. ascertained history of at least one of the following conditions: acute myocardial infarction, stroke, angina, diabetes, peripheral artery disease, previous by-pass intervention, percutaneous transluminal coronary angioplasty intervention). In particular, a history of acute myocardial infarction and/or stroke was registered in 259 and 64 of 874 patients with valid registered medical histories (29.6% and 7.3%), respectively. At baseline, 56.2% of subjects with a valid body mass index assessment (483 out of 860) were found to be overweight (BMI between 25-30 Kg/m^2 for men, and between 23.8-30 Kg/m^2 for women), while another 25% (n=215) were obese (BMI >30 Kg/m^{2}for both men and women. There was only a partial achievement of target levels of blood cholesterol and triglycerides in the

Table I. *Patient characteristics at baseline.*

Variable	Total number of subjects – n.	(%)
Total number of subjects	877	(100.0)
Sex (n=877) - n. (%)		
Men	483	(55.1)
Women	394	(44.9)
Age, years (n=877) – Mean (± SD)	66.0	(9.9)
Age classes (n=877) – n. (%)		
< 40 yrs	14	(1.6)
≥40-<50 yrs	32	(3.6)
≥50-<60 yrs	171	(19.5)
≥60-<70 yrs	323	(36.8)
≥70-<80 yrs	276	(31.5)
≥ 80 yrs	61	(7.0)
Family status (n=860) – n. (%)		
Married/in a relationship	665	(77.3)
Single	40	(4.7)
Separated	7	(0.8)
Widower/widow	148	(17.2)
School education (n=817) – n. (%)		
None	52	(6.4)
Primary school	317	(38.8)
Middle school	170	(20.8)
Secondary school	201	(24.6)
University degree	77	(9.4)
Type of prevention (n=877) – n. (%)		
Primary	235	(26.8)
Secondary	642	(73.2)
Risk factors – smoking (n=831) - n. (%)		
Smokers	175	(21.1)
Ex-smokers	250	(30.1)
Non-smokers	406	(48.9)
Family history of CV disease (n=805) - n. (%)		
Yes	391	(48.6)
No	414	(51.4)
Hypertension (n=866) - n. (%)		
Yes	675	(77.9)
No	191	(22.1)
Hypercholesterolemia (n=875) - n. (%)		
Yes	765	(87.4)
No	110	(12.6)
Diabetes (n=807) - n. (%)		
Yes	261	(32.3)
No	546	(67.7)
Hypertriglyceridemia (n=874) - n. (%)		
Yes	388	(44.4)
No	486	(55.6)

cohort. In particular, more than 50% and 35% of subjects, respectively, had total cholesterol and LDL cholesterol levels above the acceptable threshold. The percentage of patients reaching the clinical targets for the other lipid parameters was generally higher (range 77-82%).

Utilization of lipid-lowering drugs

Of the 877 subjects included in the study, 839 (95.7%) had at least one prescription of lipid-lowering drugs in both phases of the study (before and after the GP education program). Table II illustrates the distribution of patients according to

Table II. *Drug utilization of lipid-lowering drugs and concomitant CV medications.*

Variable	Total number of subjects – n.	(%)
Total number of subjects	839	(100.0)
Type of lipid-lowering drugs*		
C10AA – HMG CoA reductase inhibitors (statins)	801	(95.5)
C10AB – Fibrates	22	(2.6)
C10AC – Bile acid sequestrants	10	(1.2)
C10AX – Other lipid- modifying agents	94	(11.2)
C10BA – Statins in combination with other drugs	24	(2.9)
Use of concomitant CV medications*		
Anti-diabetic drugs	280	(33.4)
Antithrombotic agents	587	(70.0)
Anti-hypertensive drugs (all types)	698	(83.2)
Adherence to statin treatment (n=729)		
MPR <25%	10	(1.4)
25%≤MPR<50%	76	(10.4)
50%≤MPR<80%	201	(27.6)
MPR ≥80%	442	(60.6)

**The sum of percentages in this group can exceed 100%, as the same subjects could receive two or more different drugs.*

Table III. *Biochemical test and other risk assessment record rates: comparison between the periods before and after the educational program.*

Variable	Before	After	
	Total number of subjects – n. (%)		p value
Total number of subjects	877 (100.0)	877 (100)	-
Lipid assessment			
Total cholesterol	850 (96.9)	855 (97.5)	0.2551
LDL cholesterol	786 (89.6)	787 (89.7)	0.9224
HDL cholesterol	817 (93.2)	808 (92.1)	0.2272
Triglycerides	842 (96.0)	852 (97.1)	0.0424
Other risk factors assessment			
Blood pressure	872 (99.4)	852 (97.1)	0.0000
Glycaemia	813 (92.7)	835 (95.2)	0.0005
Body Mass index	860 (98.1)	870 (99.2)	0.0003
Smoking habits	831 (94.8)	772 (88.0)	0.0000

prescribed lipid-lowering drugs and concomitant medications for cardio-cerebrovascular disease. The majority of patients treated with lipid-lowering drugs received statins (n= 801; 95.5%). Analyses of concomitant medications highlighted the high prevalence of anti-hypertensive and anti-thrombotic drug use. This is consistent with the large number of patients having an ascertained history of major

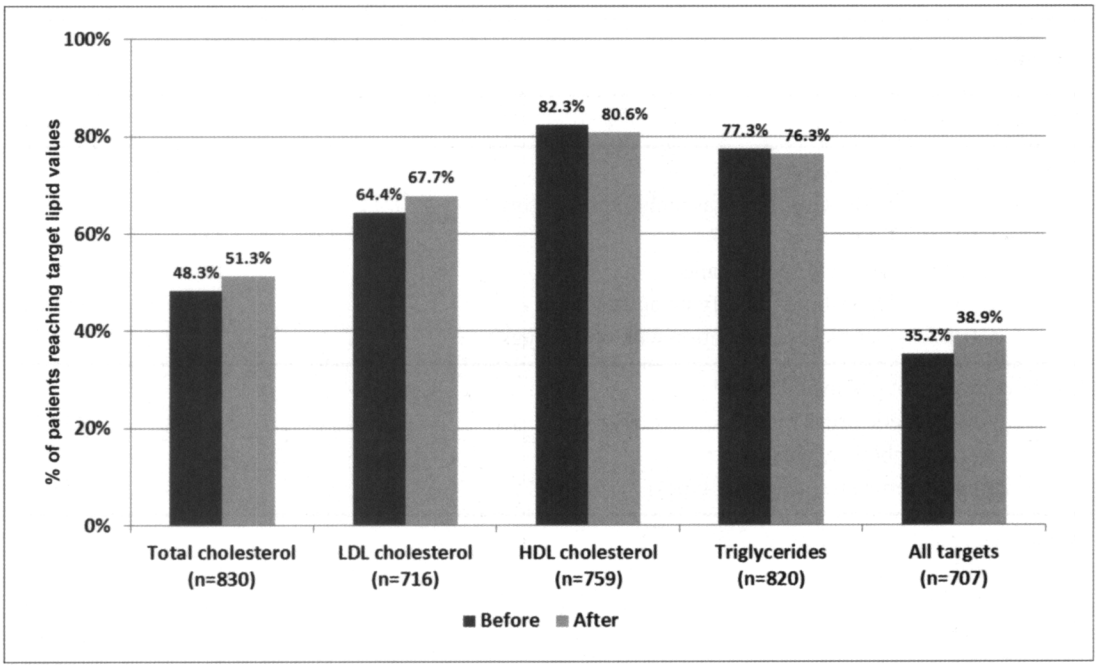

Fig. 3. *Achievement of lipid targets: comparison between periods preceding and following the program. p value not significant for all comparisons [Chi-squared test for pairwise data (after vs before training program)]*

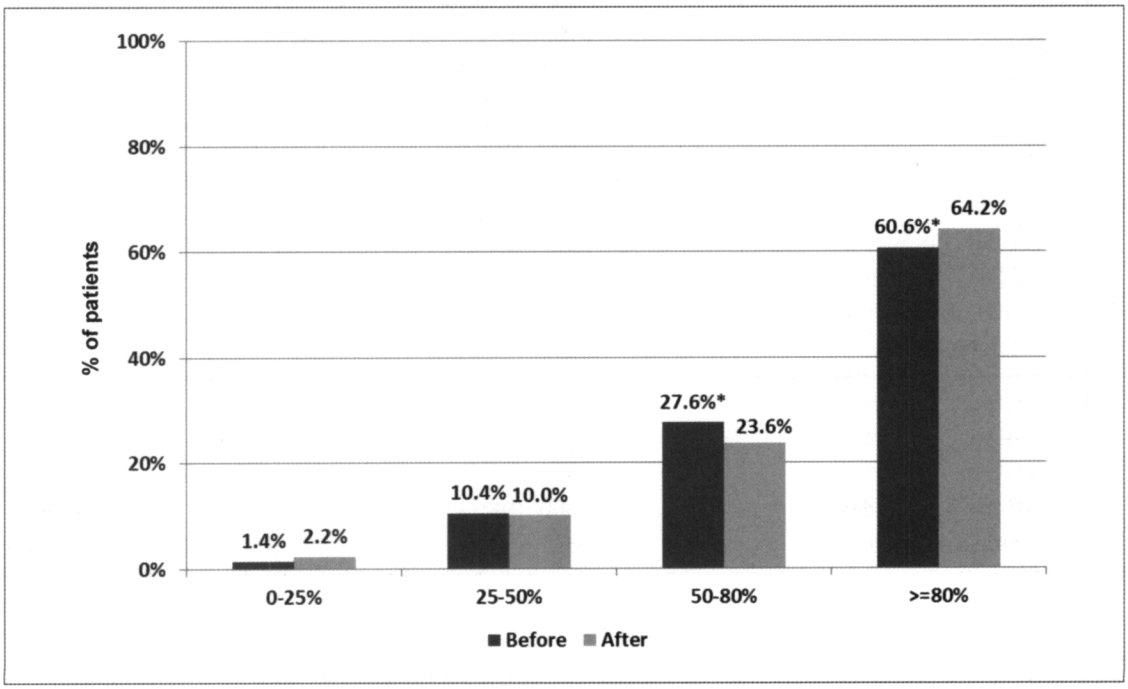

Fig. 4. *Statin adherence: comparison between periods preceding and following the program. *p<0.05 [Chi-squared test for pairwise data (after vs before training program)].*

cardio-cerebrovascular events.

The medication possession ratio was calculated for those patients chronically treated with statins (i.e. patients for whom the time elapsed between the first and the last prescribed prescription was ≥28 days). The distribution of chronic statin users according to level of adherence is reported in Table II. Excluding patients with non-continuous statin treatment, the level of statin adherence was quite high, with only 11.8% of subjects with <50% medication coverage.

Effects of the GP training program on healthcare indicators

At the end of the study, the healthcare indicators measured during the two phases of the study were compared to each other to determine whether the training program offered to GPs provided some benefit. Fig. 3 shows the achievement of different blood lipid targets (total cholesterol, LDL cholesterol, HDL cholesterol, triglycerides) in the two phases. In the subgroup of patients with blood lipid measurements in both periods, no significant improvement was seen in the period following the program compared to the period before. Overall, the percentages of patients achieving the target outcomes were similar across the two periods ($p>0.05$ for all *chi*-squared test for the pairwise comparisons). No statistically significant differences in the achievement of lipid targets were detected when stratifying the analysis by sex and type of prevention. Similarly, there were no differences in the achievement of target blood pressure values comparing the period preceding (n=424; 50.1%) and that following (n=400; 47.3%; p=0.2431) the GP training program. Neither the relative frequency of obese nor that of overweight and obese patients decreased after the education program compared to before (obese patients: 25% *vs* 26%, p=0.6187; overweight and obese patients: 81.2% *vs* 81.5%, p=0.8527). Patient smoking status remained almost unchanged, with non-smoking subjects (never smokers and ex-smokers) numbering 588 (80.2% of evaluable population, n=733) after the program, *vs* 572 (78%; p=0.3038, *chi*-squared test for the pairwise comparison) before the program.

Fig. 4 illustrates distribution of adherence among patients in the two study periods, calculated using the medication possession ratio. A slight but statistically significant improvement of MPR was registered after the educational program. The evaluation was carried out for chronic statin users who were treated before and after the educational program. While the percentage of subjects with MPR<0.25 and 0.25≤MPR<0.5 remained the same after and before the program (MPR<0.25: after=2.2% *vs* before=1.4%, p=0.1409; 0.25≤MPR<0.5: after=10.0% *vs* before=10.4%, p=0.7188), the percentage of subjects with 0.5≤MPR<0.8 decreased (after=23.6% *vs* before=27.6%, p=0.0110) while there was an increase in patients with an MPR≥0.8 (after=64.2% *vs* before=60.6%, p=0.0426).

A univariate regression analysis was conducted to estimate the association of statin adherence with the achievement of target total blood cholesterol (<200 mg/dl). Moderate (OR= 2.7 for 0.5≤MPR<0.8 *vs* MPR<0.5, 95% CI: 1.3-5.7) and high levels of statin adherence (OR= 3.3 for MPR≥0.8 *vs* MPR<0.5, CI 95%: 1.7-6.7) were found to be associated with the achievement of total cholesterol target. A similar association was found for the achievement of the blood LDL cholesterol target (<130 mg/dl). Both moderate (OR= 3.0 for 0.5≤MPR<0.8 *vs* MPR<0.5, 95% CI: 1.3-6.7) and high levels of statin adherence (OR= 3.3 for MPR≥0.8 *vs* MPR<0.5, CI 95%: 1.5-7.2) predicted achievement of the blood LDL therapeutic target.

Finally, some process indicators were measured to assess the quality of care provided by GPs through the monitoring of relevant laboratory parameters and potential risk factors on a regular basis. Table III shows the main results of this analysis. Although the number of subjects with at least one clinical test over the observation periods increased after the educational program compared to the pre-program phase, this variation did not represent a significant improvement in the quality of care since the average clinical test rates for cholesterol, blood pressure, blood sugar, BMI, and smoking habits were already high (>90%) in the period preceding the educational program.

DISCUSSION

Education in primary care plays a central role in managing the prevention of cardio-cerebrovascular diseases. Combined audit-feedback approaches represent an important tool to monitor and improve

the quality of healthcare service and to promote adherence to clinical guidelines. The present study is an example of this process applied to lipid-lowering management.

The final results of this study suggest some relevant conclusions. Although GPs monitor lipid parameters and other relevant clinical and risk factors indicators (blood pressure, body mass index, smoking habits, etc.) on a regular basis (monitoring rates were >90% in both the phases of the study), rates of target achievements were not very satisfactory. After the educational program and with regard to the four lipid parameters investigated, target achievement varied from a minimum of 51.3% (total cholesterol) to a maximum of 80.6% (HDL cholesterol). Moreover, there was no statistical evidence that the educational program resulted in an improvement in the achievement of the pre-defined clinical targets. However, baseline lipid parameter control was relatively high compared to other epidemiological studies (26, 27) and this in itself may limit the potential for improvement. This is consistent with Jamtvedt et al. who claim that the absolute effects of audit and feedback are more likely to be large when baseline adherence to recommended practice is low (13). Moreover, in our study all patients were already receiving lipid-lowering drugs before the beginning of the study. As a consequence, most of them are expected to have already achieved a reduction in lipid parameters and yet further reduction is hard to obtain.

The modification of other risk factors, such as weight and smoking habits was even harder to achieve. The study confirms a well-established trend, according to which patients are unlikely to change their dietary life-style. About 80% of subjects enrolled in this study remained overweight throughout the study. Although the overall level of CCV risk of the enrolled population was extremely high (73.2% of the sample had a medical history of major cardiovascular events), about 20% of subjects were still smoking by the end of the observation period.

Patients' adherence to statin therapy is partially satisfactory. Nevertheless, results show a higher trend of adherence than other previous studies on statins carried out in Italy using a similar methodology (28). This finding may limit the potential and may justify the low efficacy of the educational program to improve adherence. However, a slight but significant increase in patients' adherence to statin therapy was observed. Moreover, the study confirmed a statistically significant association between statin adherence and achievement of lipid targets, in line with several previous findings (29, 30). Nevertheless, there is still a non-negligible quota of patients not taking statins continuously or having a low threshold of adherence (MPR<80%).

Some limitations of this study should be taken into account. Findings of this survey may not be generalizable to the general primary care setting because GPs participating in this research: i) participated on a voluntary basis; ii) had already been involved in regular clinical research activity, which is not a standard practice for Italian general practitioners. For these reasons, we believe these results could overestimate the quality of clinical care and the achievement of clinical outcomes and risk factors, compared to standard clinical practice.

General practice databases, such as Arianna, provide clinical data from large populations and preclude the influence of biases such as selection bias. However, even adding details from a dedicated CRF, it was not possible to collect data on other potentially relevant indicators such as inflammatory markers, blood leukocyte or analysis of vascular tissue, because most of the general practitioners do not record that kind of data in their daily clinical practice. As a consequence, the pleiotropic effects of statins could not be investigated.

Moreover, the overall study results suggest that the education program was partially effective in improving the achievement of clinical targets and the management of risk factors in patients at risk of CCV. This result may be explained by the following hypotheses.

Firstly, the program was mainly aimed at updating GPs about the recent findings and recommendations on lipid-lowering measures. In other words, the program was a scientific update of the evidence in this area. Although this aspect is crucial for disease management, final results of the study suggest that other factors may have an equally important role in the GP education and disease management. For example, it is likely that educational programs in primary care, including the one implemented in this

study, should be more focused in helping general practitioners to communicate effectively with their patients and to convince them to adhere to medical prescriptions and recommendations as best as they can. In particular, lipid control is strictly related to drug adherence and modifications of life-style habits, two of the most challenging objectives in day-to-day patient management.

Secondly, the educational program covered a single day of activities. It is possible that a more structured and multi-disciplinary approach, targeting different topics (scientific update, local adaptation of recent clinical guidelines, communication to the patients, development of PC-assisted tools to monitor patients' adherence to medical prescriptions and recommendations, set-up of non-pharmacological strategies to correct life-style habits) over a longer period of time would be more effective in improving lipid-related CCV risk minimization in the future. Of course, such an approach would require significant investments from the Local Health Unit. Therefore, further research should aim to target not only the potential achievable improvements in primary care, but also the cost-effectiveness of the interventions themselves.

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