

Practice setting and secondary prevention of coronary artery disease

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Abstract

Introduction: Patients with established coronary artery disease (CAD) are at high risk of recurrent cardiovascular events. The aim of the analysis was to compare time trends in the extent to which cardiovascular prevention guidelines have been implemented by primary care physicians and specialists.

Material and methods: Five hospitals with cardiology departments serving the city and surrounding districts in the southern part of Poland participated in the study. Consecutive patients hospitalized due to an acute coronary syndrome or for a myocardial revascularization procedure were recruited and interviewed 6–18 months after hospitalization. The surveys were carried out in 1997–1998, 1999–2000, 2006–2007 and 2011–2013.

Results: The proportion of smokers increased from 16.0% in 1997–1998 to 16.4% in 2011–2013 among those who declared that a cardiologist in a hospital outpatient clinic decided about the treatment, from 17.5% to 34.0% ($p < 0.01$) among those treated by a primary care physician, and from 7.0% to 19.7% ($p = 0.06$) among patients treated in private cardiology practices. The corresponding proportions were 44.6% and 42.4% ($p < 0.01$), 47.7% and 52.8% ($p = 0.53$), 44.2% and 42.2% ($p = 0.75$) for high blood pressure, and 42.5% and 71.2% ($p < 0.001$), 51.4% and 79.6% ($p < 0.001$), 52.4% and 72.4% ($p < 0.01$) for LDL cholesterol level not at recommended goal. The proportion of patients prescribed cardioprotective medications increased in every analyzed group.

Conclusions: The control of cardiovascular risk in CAD patients has only slightly improved since 1997/98 in all health care settings. The greatest potential for further improvement was found among patients whose post-hos-

pital care is provided by primary care physicians. It is associated with promotion of a no-smoking policy and enhanced prescription of guideline-recommended drugs.

Key words: coronary artery disease, secondary prevention, cardiovascular risk, smoking, cholesterol, blood pressure.

Introduction

Patients with established coronary artery disease (CAD) are at high risk of recurrent cardiovascular events. Despite advances in pharmacological and invasive treatment methods, risk factors remain independent predictors of cardiovascular mortality in CAD patients [1]. Smoking cessation, providing advice on diet and physical activity and ensuring optimal pharmacological treatment are crucial factors in reducing mortality in patients who have suffered from myocardial infarction [2]. Thus, in the case of preventive cardiology the highest priority has been given to patients with established CAD [3].

The Cracovian Program for Secondary Prevention of Ischaemic Heart Disease was launched in 1997. The main goal of the program was to assess and improve the quality of clinical care in the secondary prevention of CAD in Krakow. The first results showed insufficient implementation of CAD prevention guidelines in clinical practice and considerable potential for a further reduction of cardiovascular risk in CAD patients [4]. The same hospitals participated in surveys in 1999–2000, 2006–2007 and 2011–2013 [5–8], which similarly to the EUROASPIRE surveys [9–11] evaluated the implementation of cardiovascular prevention guidelines.

Polish society has undergone profound changes triggered by the change of the political system in 1989 and by entering the European Union in 2004. Poland's healthcare system has been in transition for the last 20 years, both in terms of institutional changes and regulations regarding drug registration, prescription, and reimbursement. More specifically, the relative position of primary care physicians in regard to specialists has evolved.

Therefore, our aim was to compare time trends in the extent to which cardiovascular prevention guidelines have been implemented by primary care physicians and specialists.

Material and methods

The study participants and the methods used have been described in previous reports [4–8]. A brief description relevant to the presented analysis is given below.

Five hospitals serving the city and surrounding districts in southern Poland participated in the sur-

veys. The total population of this area is approximately 1 200 000. In each cardiac department the medical records were reviewed and consecutive patients hospitalized due to acute myocardial infarction, unstable angina, or percutaneous coronary intervention (PCI), or scheduled for coronary artery bypass grafting (CABG), were identified retrospectively, excluding those who had died during their in-hospital stay. Participants were invited to attend a follow-up examination 6 to 18 months after their discharge. The patients who declared they had no regular health check-ups after the discharge from the hospital were excluded from the present analysis. The surveys were carried out in 1997–1998, 1999–2000, 2006–2007 and 2011–2013.

Data on demographic characteristics, patients' personal history of CAD, smoking status, blood pressure, fasting glucose, plasma lipids, and prescribed medications were obtained using a standardized data collection form. Patients' height and weight were measured in a standing position without shoes and heavy outer garments using standard scales with a vertical ruler. The body mass index (BMI) was calculated according to the following formula: $BMI = \text{weight [kg]} / (\text{height [m]})^2$. Blood pressure was measured twice, on the right arm in a sitting position after at least 5 min of rest. For plasma lipid and glucose measurements a fasting venous blood sample was taken between 7.30 and 8.30 in the morning.

The secondary prevention coefficient was calculated as follows: for each risk factor controlled (non-smoker, blood pressure $< 140/90$ mm Hg, low-density lipoprotein (LDL) cholesterol at recommended goal (< 3.5 mmol/l in 1997–1998 [12], < 3.0 mmol/l in 1999–2000 [13], < 2.5 mmol/l in 2006–2007 [14], and < 1.8 mmol/l in 2011–2013 [3, 15]), fasting glucose < 7.0 mmol/l, BMI < 30 kg/m 2 during the follow-up interview) one point was given. Additionally, one point was awarded for taking an antiplatelet or an antithrombotic agent, one point for taking an angiotensin convertase enzyme (ACE) inhibitor or a sartan, and one point for taking a β -blocker in patients with heart failure or myocardial infarction in the history. Thus, the secondary prevention coefficient could vary from 1 to 8.

For the purposes of the present analysis the study participants were grouped according to their answers to the question: "Who decides about your treatment?"

Statistical analysis

Categorical variables were reported as percentages and continuous variables as means \pm standard deviation. The Pearson χ^2 test was applied to all categorical variables. Normally distributed continuous variables were compared using Student's *t* test or analysis of variance. Variables without normal distributions were evaluated using the Mann-Whitney *U* test or the Kruskal-Wallis analysis of variance. Multivariate analyses were performed using the generalized linear model as implemented in the Statistica 8.0 software (StatSoft INC., Tulsa, USA). A two-tailed *p*-value of less than 0.05 was regarded as statistically significant.

Results

Overall, the data of 1924 patients (408 studied in 1997–1998, 419 in 1999–2000, 497 in 2006–2007, and 600 in 2011–2013) were included to the present analysis. Mean age of the participants of the first, second, third and fourth surveys was 57.9 ± 8.3 , 58.7 ± 8.1 , 62.3 ± 8.9 , and 64.8 ± 8.8 years (*p* < 0.05), respectively. The proportions of women were 27.0%, 30.8%, 30.0%, and 35.3% (*p* < 0.05), respectively. There was no significant difference in the mean duration of education (11.3 ± 3.6 , 11.6 ± 3.5 , 11.6 ± 3.4 and 11.9 ± 3.2 , respectively). Out of 408 participants of the first survey, 188 (46.1%) declared that their treatment had been decided by a cardiologist or physician in a hospital outpatient clinic, another 177 (43.4%) reported that the decisions had been made by a primary care physician and 43 (10.5%) by a physician in a private cardiology practice. The corresponding numbers in the second survey were 149 (35.6%), 232 (55.4%) and 38 (9.1%), in the third survey 268 (53.9%), 172 (34.6%) and 57 (11.5%), whereas in the last survey the figures were 481 (80.2%), 53 (8.8%) and 66 (11.0%). The characteristics of the participants according to practice setting are presented in Table I. Patients who declared that a general practitioner had decided on their treatment were significantly younger, less educated, were more often professionally active, more often had undergone CABG and less often PCI as index events compared to the other study groups. Based on their hospital records, patients who declared that their treatment had been planned by a general practitioner were more often smokers and suffered less often from dyslipidemia or obesity (Table I). These patients were less frequently prescribed antiplatelets, β -blockers, ACE inhibitors or sartans, and lipid-lowering agents on their discharge from the hospital.

The proportions of patients with non-controlled risk factors 6–18 months after discharge are presented in Table II. The participants of the third and

fourth surveys were significantly more likely to be smokers compared to the first and second surveys. The time trends were similar in all three analyzed groups (the interaction between groups and surveys was not significant (*p* = 0.68)). In general, those patients who reported that a general practitioner had decided about their treatment were more frequently smokers in the post-discharge period compared to other groups. We repeated all the analyses after smoking in the pre-hospitalization period had been included in the statistical model, and we found very similar results (data not shown).

We did not find any evidence of different time trends (*p*-value for the interaction: 0.24) in blood pressure control between the analyzed groups (Table II). We repeated all the analyses after including hypertension as diagnosed during the index hospitalization in the statistical model, and we found very similar results (data not presented).

The proportions of patients with LDL cholesterol level not at goal differed between surveys both when we analyzed all participants as well as when we limited the analysis to specific groups (Table II). The time trends did not differ significantly between the analyzed groups (*p* = 0.62). We repeated all the analyses after including dyslipidemia as diagnosed during the index hospitalization in the statistical model, and we found very similar results (data not shown). When we applied the currently recommended treatment goal (LDL cholesterol < 1.8 mmol/l), we found a significant improvement in the control of LDL cholesterol level: 4.1% in the first survey, 1.2% in the second survey, 22.1% in the third, and 27.9% in the fourth survey (*p* < 0.001). We found similar time trends when we analyzed specific groups: 6.1% vs. 1.4% vs. 22.9% vs. 28.8% (*p* < 0.001) in the case of those who declared that a cardiologist or a physician in a hospital outpatient clinic had decided about their treatment, 2.3% vs. 1.3% vs. 18.3% vs. 20.4% (*p* < 0.001) in participants who declared that a primary care physician had decided about the treatment, and 2.5 vs. 0.0% vs. 29.8% vs. 27.6% (*p* < 0.001) in patients treated in private cardiology practices.

We found increasing proportions of study participants who were obese (*p*-value for interaction between surveys and groups: 0.20). Although the proportion of patients with fasting glucose ≥ 7.0 mmol/l increased significantly, only in those who declared that a cardiologist or physician in a hospital outpatient clinic had decided about their treatment was the interaction between surveys and groups not significant (*p* = 0.77). We repeated all the analyses after the presence of diabetes and obesity during the index hospitalization had been included in the statistical model, and we found very similar results (data not shown).

The proportions of patients taking cardioprotective medications are presented in Table III. We found significant differences between the surveys for every studied drug class. We also observed a significant increase in the use of statins in the group as a whole (19.9% vs. 34.6% vs. 84.9% vs. 84.7%, $p < 0.001$) as well as when we analyzed specific groups: 36.2% vs. 48.3% vs. 84.6% vs. 86.9% ($p < 0.001$) in the case of those who declared that a cardiologist or physician in a hospital outpatient clinic decided about the treatment, 5.1% vs. 27.6% vs. 86.6% vs. 69.8% ($p < 0.001$) in the case of participants who declared that a primary care physician had decided about their treatment, and 9.3% vs. 23.7% vs. 80.7% vs. 80.3% ($p < 0.001$) in the case of patients treated in pri-

vate cardiology practices. The use of fibrates decreased in the group as a whole (14.0% vs. 7.9% vs. 3.9% vs. 2.3%, $p < 0.001$) as well as when we analyzed specific groups: 12.2% vs. 8.7% vs. 5.3% vs. 2.1% ($p < 0.001$) in the case of those who declared that a cardiologist or a physician in a hospital outpatient clinic had decided about the patient's treatment, 13.6% vs. 6.9% vs. 2.3% vs. 3.8% ($p < 0.001$) in the case of participants who declared that a primary care physician decided about their treatment, and 23.3% vs. 10.5% vs. 1.8% vs. 3.0% ($p < 0.001$) in the case of patients treated in private cardiology practices. The time trends in the analyzed groups were similar with the exception of lipid-lowering agents (p -value for the interaction between surveys and groups:

Table I. Characteristics of the study group by site of care provided after hospitalization

Parameter	Practice setting			<i>P</i> -value	Total <i>N</i> = 1924
	Hospital outpatient clinic /cardiologist <i>N</i> = 1086	General practitioner <i>N</i> = 634	Private cardiology practice <i>N</i> = 204		
Age [years]	61.8 ±9.2	60.5 ±8.7	61.5 ±8.9	0.01	61.4 ±9.0
Sex (%):				0.07	
Men	67.2	72.2	66.7		68.8
Women	32.8	27.8	33.3		31.2
Duration of education [years]	11.7 ±3.4	11.1 ±3.3	12.7 ±3.9	< 0.001	11.6 ±3.4
Professionally active (%)	20.8	19.7	31.9	< 0.01	21.6
Index event (%):				< 0.001	
Myocardial infarction	26.4	29.0	33.3		28.0
Unstable angina	26.2	27.0	27.9		26.6
PCI	32.0	19.2	24.5		27.0
CABG	15.5	24.8	14.2		18.4
Hospitalization in (%):				< 0.001	
Teaching hospital	60.5	46.4	43.1		54.0
Non-teaching hospital	39.5	53.6	56.9		36.0
Smoking (%)*	24.9	34.5	23.5	< 0.001	27.9
Hypertension (%)**	74.7	69.7	70.6	0.07	72.6
Dyslipidemia (%)**	69.7	58.2	61.3	< 0.001	64.0
Diabetes (%)**	24.3	22.4	20.6	0.42	23.3
Obesity (%)**	21.1	15.9	17.7	0.03	19.0
Drugs (%):***					
Antiplatelets	96.4	91.9	94.6	< 0.001	94.7
β-blockers	81.3	74.2	75.0	< 0.01	78.3
ACE inhibitors/sartans	76.0	65.9	70.6	< 0.001	72.1
Lipid-lowering drugs	77.5	55.7	68.1	< 0.001	69.3

*Within 1 month before index hospitalization, **diagnosed during index hospitalization, ***prescribed at discharge. PCI – percutaneous coronary intervention, CABG – coronary artery bypass grafting.

Table II. Proportions of patients with non-controlled risk factors 6–18 months after discharge. The differences were adjusted for age, sex, education, professional activity, hospital setting, and index event

Variable	Practice setting			P-value	Total
	Hospital outpatient clinic /cardiologist	General practitioner	Private cardiology practice		
Smoking:					
1997–1998 (%)	16.0	17.5	7.0	0.12	15.7
1999–2000 (%)	12.1	18.5	7.9	0.12	15.3
2006–2007 (%)	16.4	23.8	17.5	0.05	19.1
2011–2013 (%)	16.4	34.0	19.7	0.30	18.3
P-value	< 0.01	< 0.01	0.06		< 0.001
All (%)	15.8	21.0	14.2	0.02	
Blood pressure ≥ 140/90 mm Hg:					
1997–1998 (%)	44.6	47.7	44.2	0.69	45.9
1999–2000 (%)	53.0	47.8	55.3	0.25	50.4
2006–2007 (%)	50.4	45.3	41.1	0.38	47.6
2011–2013 (%)	42.4	52.8	42.2	0.31	43.3
P-value	< 0.01	0.53	0.75		0.06
All (%)	46.3	47.5	44.8	0.97	
LDL cholesterol not at goal*:					
1997–1998 (%)	42.5	51.4	52.4	0.73	47.5
1999–2000 (%)	59.6	70.6	65.8	0.34	66.3
2006–2007 (%)	38.9	41.4	33.3	0.78	39.1
2011–2013 (%)	71.2	79.6	72.4	0.36	72.1
P-value	< 0.001	< 0.001	< 0.01		< 0.001
All (%)	56.3	58.0	55.4	0.75	
BMI ≥ 30 kg/m ² :					
1997–1998 (%)	25.9	27.6	9.3	0.03	24.9
1999–2000 (%)	30.2	25.0	28.9	0.19	27.2
2006–2007 (%)	32.6	34.1	35.7	0.49	33.5
2011–2013 (%)	34.5	28.3	34.8	0.89	34.0
P-value	0.26	0.15	0.02		< 0.01
All (%)	32.0	28.5	28.6	0.37	
Fasting glucose ≥ 7.0 mmol/l:					
1997–1998 (%)	6.9	12.4	12.2	0.18	9.8
1999–2000 (%)	11.0	16.3	5.3	0.30	13.4
2006–2007 (%)	13.0	13.7	10.7	0.82	13.0
2011–2013 (%)	16.2	16.3	10.3	0.62	15.6
P-value	0.01	0.69	0.79		0.09
All (%)	13.0	14.5	9.4	0.39	

BMI – body mass index.

Table III. Proportions of patients taking cardioprotective drugs 6–18 months after discharge. The differences were adjusted for age, sex, education, professional activity, hospital setting, and index event

Variable	Practice setting			<i>P</i> -value	Total
	Hospital outpatient clinic /cardiologist	General practitioner	Private cardiology practice		
Antiplatelet:					
1997–1998 (%)	83.5	72.9	67.4	0.25	77.2
1999–2000 (%)	91.9	85.8	81.6	0.26	87.6
2006–2007 (%)	89.1	90.0	94.7	0.44	90.1
2011–2013 (%)	90.9	88.7	92.4	0.70	90.8
<i>P</i> -value	< 0.01	< 0.01	< 0.01		< 0.001
All (%)	89.3	83.5	85.8	0.03	
β-blocker:					
1997–1998 (%)	65.4	54.2	62.8	0.51	60.3
1999–2000 (%)	67.8	62.5	65.8	0.98	64.7
2006–2007 (%)	86.1	89.5	84.2	0.41	87.1
2011–2013 (%)	81.7	71.7	84.8	0.11	81.2
<i>P</i> -value	< 0.001	< 0.001	0.01		< 0.001
All (%)	78.0	68.3	76.5	< 0.01	
ACE inhibitor/sartan:					
1997–1998 (%)	42.0	49.7	53.5	0.44	46.6
1999–2000 (%)	50.3	45.3	55.3	0.17	48.0
2006–2007 (%)	79.3	80.1	78.9	0.82	79.6
2011–2013 (%)	78.8	77.4	69.7	0.27	77.7
<i>P</i> -value	< 0.001	< 0.001	0.02		< 0.001
All (%)	68.6	58.6	66.2	< 0.01	
Lipid-lowering agent:					
1997–1998 (%)	48.9	18.6	32.6	< 0.001	34.1
1999–2000 (%)	57.0	34.5	34.2	0.02	42.5
2006–2007 (%)	86.8	87.1	80.7	0.43	86.2
2011–2013 (%)	87.1	69.8	80.3	< 0.01	84.8
<i>P</i> -value	< 0.001	< 0.001	< 0.001		< 0.001
All (%)	76.3	47.2	61.8	< 0.001	

antiplatelets 0.36, β-blockers 0.25, ACE inhibitors/sartans 0.25, lipid-lowering drugs < 0.001). The results did not change significantly when prescribed drugs at discharge from the index hospitalization were included in the statistical model (data not presented).

Table IV presents the values of the secondary prevention coefficient by survey and practice set-

ting. When adjusted for confounding variables, the coefficient changed over time (Table IV). The interaction between surveys and groups was not significant (*p* = 0.49), thus suggesting a similar relationship between the surveys in each analyzed group. The results did not change significantly when the presence of risk factors during the index hospitalization and the prescribed drugs at

Table IV. Secondary prevention coefficient by survey and practice setting. The differences were adjusted for age, sex, education, professional activity, hospital setting, and index event

Antiplatelet	Practice setting			P-value	Total
	Hospital outpatient clinic /cardiologist	General practitioner	Private cardiology practice		
1997–1998	5.22 ±1.29	5.10 ±1.25	5.41 ±1.05	0.24	5.19 ±1.25
1999–2000	5.18 ±1.25	4.90 ±1.25	5.24 ±1.38	0.48	5.03 ±1.27
2006–2007	5.87 ±1.28	5.61 ±1.26	5.89 ±1.14	0.28	5.78 ±1.26
2011–2013	5.37 ±1.29	4.91 ±1.06	5.37 ±1.25	0.03	5.33 ±1.27
P-value	< 0.001	< 0.001	0.05		< 0.001
All	5.45 ±1.31	5.15 ±1.27	5.50 ±1.22	< 0.001	

discharge from the index hospitalization where included in the statistical model (data not shown).

Discussion

In general, despite the passing of two decades, our results showed a considerable potential for a further reduction in cardiovascular risk following hospitalization for CAD. The potential for further decreasing cardiovascular risk in CAD patients has only slightly fallen since 1997/98. Although we found a higher rate of smoking in patients who declared that a primary care physician decided about their treatment, even when multivariate adjustments were made, it should be underlined that unidentified differences between the analyzed groups could be responsible for the difference. We found no major difference in the control of other risk factors between the groups defined by the site of care.

Importantly, we found similar changes in the implementation of the preventive guidelines irrespectively of the practice setting. Indeed, control of risk factors and the use of cardioprotective medications changed similarly regardless of whether the patients were treated in hospital outpatient clinics, by primary care physicians or by cardiologists in their private practices.

According to the recent AMI-PL report, the average number of visits to a primary care clinic made by survivors of myocardial infarction was 7.7 per year in 2012, whereas the average number of consultations with a cardiologist was 1.8 per year [16]. Although we found that the majority of the last survey participants declared that their treatment had been decided by a cardiologist, these results should not be seen as contradictory. Rather, our results suggest that in the opinion of patients with CAD most primary care physicians do not change therapy prescribed by a cardiologist. Indeed, it seems patients with CAD recognize now that the treatment prescribed at discharge from

the hospital usually is not modified during the following months. This may also explain the relatively small difference in the service quality provided by cardiologists and primary care physicians. In addition, our results may confirm the decreasing esteem of primary care providers among coronary patients in Poland. It should also be noted that in contrast to the AMI-PL report, we included not only patients who had experienced an acute coronary syndrome but also patients who had undergone planned revascularization procedures.

We found the secondary prevention coefficient to be significantly lower in 2011–2013 as compared with 2006–2007. This difference does not necessarily indicate a decline in the quality of medical care in the field of secondary prevention, as the difference was mainly driven by the difference in the proportions of patients with LDL cholesterol at recommended goal. Indeed, the recommended goal of lipid-lowering therapy in 2006–2007 was LDL cholesterol below 2.5 mmol/l, whereas from 2011 the goal was < 1.8 mmol/l. It is possible that the information about the new goal did not spread fast enough. Another explanation might be the well-known therapeutic inertia [17]. In contrast to common beliefs, our results do not support the opinions on significantly shorter delays in spreading new guidelines among cardiologists as compared to primary care physicians. It is also possible that knowledge about side-effects of therapy could prevent physicians from prescribing and patients from taking drugs, especially in high doses [18–20]. Another possible explanation for the decrease in the secondary prevention coefficient in 2011–2013 could be a slightly lower participation rate compared to previous surveys [4–6, 8]. It is possible that patients in better condition could decide more often not to participate in the survey.

We are unaware of any study published in recent years which was designed to compare secondary prevention of CAD in different practice

settings in Poland. However, recent evidence suggests at least comparable potential for improvement in other parts of Poland, both in patients treated by cardiologists and those treated by primary care physicians [21–26]. This was also shown in patients undergoing bypass surgery and other forms of cardiovascular disease [27]. It should be stressed that the prescription rates for cardiopreventive medications in Poland are similar to the average prescription rates in centers participating in the EUROASPIRE IV survey and much higher compared to centers from high-income countries participating in the PURE study [11, 28].

Organizational interventions for the secondary prevention of CAD have been shown to reduce mortality in CAD patients [29]. Many experts suggest the need to implement educational programs in clinical practice [24, 30]. Recently, experts of the Polish Cardiac Society described a new organizational system (named “Optimal Model of Comprehensive Rehabilitation and Secondary Prevention”), involving both exercise-based rehabilitation and education intervention, the widespread implementation of which in Poland could be related to a decrease in the number of deaths by 3389, in the number of myocardial infarctions by 3872, in the number of myocardial revascularization procedures by 13 499, and in the number of cardiac hospitalizations by 23 182 yearly [31].

The present study has some limitations. Firstly, it is possible that some unidentified differences between practice setting groups exist. These differences may have influenced the approach to secondary prevention in study participants. Secondly, we were not able to assess the impact of the differences in secondary prevention implementation on the risk of cardiovascular events. Thirdly, our study participants were not representative of all CAD patients. Participants were limited to those who had undergone an acute CAD event or a revascularization procedure. Therefore, our results should not be directly applied to other subjects. However, an important strength of our analysis is that our results are not based just on abstracted medical record data but on face-to-face interviews and examinations using the same protocol and standardized methods and instruments, including central laboratory analyses of lipids and glucose. Therefore, this analysis provides reliable information on lifestyle, risk factors, and therapeutic management for secondary prevention of CAD over the period 1997–2013.

In conclusion, the control of cardiovascular risk in CAD patients has only slightly improved since 1997–1998 in all health care settings. The greatest potential for further improvement was found among patients whose post-hospital care is provided by primary care physicians, and it is associ-

ated with promotion of a no-smoking policy and enhanced prescription of guideline-recommended drugs.

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Conflict of interest

The authors declare no conflict of interest.

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