

WHO study on Prevention of REcurrences of Myocardial Infarction and Stroke (WHO-PREMISE)

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Objective To determine the extent of secondary prevention of coronary heart disease (CHD) and cerebrovascular disease (CVD) in low- and middle-income countries.

Methods A descriptive cross-sectional survey of a sample of 10 000 CHD (85.2%) and CVD (14.8%) patients (6252 men; 3748 women) was conducted over 6 months in geographically defined areas. The mean age was 59.2 years (standard deviation (SD), 10.8). Consecutive patients were recruited from a stratified random sample of primary, secondary and tertiary care facilities in defined areas in 10 countries (Brazil, Egypt, India, Indonesia, Islamic Republic of Iran, Pakistan, Russian Federation, Sri Lanka, Tunisia and Turkey). The main outcome measures were levels of lifestyle and physiological risk factors, and the use of drugs for secondary prevention of CHD and CVD.

Findings Approximately 82%, 89% and 77% of patients were aware of the cardiovascular benefits of quitting smoking, a heart-healthy diet and regular physical activity, respectively. About half (52.5%) engaged in less than 30 minutes of physical activity per day, 35% did not follow a heart-healthy diet and 12.5% were current tobacco users. Blood pressure had been measured in 93.8% (range 71–100%), blood cholesterol in 85.5% (range 29–97%) and blood sugar in 75.5% (range 65–99%) in the preceding 12 months. The proportions who had received medications among CHD and CVD patients were: aspirin, 81.2%, 70.6%; beta-blockers, 48.1%, 22.8%; angiotensin-converting enzyme inhibitor, 39.8%, 37.8%; statins, 29.8%, 14.1%, respectively. About one-fifth of patients with CHD had undergone revascularization.

Conclusion A significant proportion of patients did not receive appropriate medications. About 47% of patients had at least two or more modifiable risk factors (smoking, physical inactivity, hypertension, diabetes or hypercholesterolaemia). There are considerable missed opportunities for prevention of recurrences in those with established CVD in low- and middle-income countries.

Keywords Myocardial ischemia/drug therapy; Cerebrovascular accident/drug therapy; Cardiovascular diseases/drug therapy; Aspirin/therapeutic use; Adrenergic beta-agonists/therapeutic use; Angiotensin-converting enzyme inhibitors/therapeutic use; Hydroxymethylglutaryl-CoA reductase inhibitors/therapeutic use; Life style; Risk factors; Developing countries (*source: MeSH, NLM*).

Mots clés Ischémie myocardique/chimiothérapie; Accident vasculaire cérébral/chimiothérapie; Cardiovasculaires, Maladies/chimiothérapie; Acide acétylsalicylique/usage thérapeutique; Sympathomimétiques beta/usage thérapeutique; Inhibiteurs dipeptidyl carboxypeptidase I/usage thérapeutique; Inhibiteurs hydroxyméthylglutaryl CoA réductases/usage thérapeutique; Style vie; Facteur risqué; Pays en développement (*source: MeSH, INSERM*).

Palabras clave Isquemia miocárdica/quimioterapia; Accidente cerebrovascular/quimioterapia; Enfermedades cardiovasculares/quimioterapia; Aspirina/uso terapéutico; betaagonistas Adrenérgicos/uso terapéutico; Inhibidores de la enzima convertidora de angiotensina/uso terapéutico; Inhibidores de la hidroximetilglutaryl-CoA reductasa/uso terapéutico; Estilo de vida; Factores de riesgo; Países en desarrollo (*fuelle: DeCS, BIREME*).

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Voir page 826 le résumé en français. En la página 826 figura un resumen en español.

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Introduction

Every year about 32 million individuals suffer acute coronary and cerebral vascular events and at least half of these occur in people with established coronary heart disease (CHD) and cerebrovascular disease (CVD) (1, 2). Patients who have suffered a stroke are at an increased risk of a further stroke, about 7% per annum (3). Similarly survivors of myocardial infarction (MI) are at an increased risk of recurrent infarctions and have an annual death rate at least five to six times higher than that of people who do not have CHD (4, 5). Systematically identifying patients who have had MI or stroke and offering them intensive preventive treatment could prevent many vascular events and deaths, improve health related quality of life and reduce the health care costs associated with invasive and expensive revascularization treatment. Thus secondary prevention of major cardiovascular disease (CVD) is recognized as a key component of a cost-effective public health strategy to reduce the rising burden of this disease (6).

Treatment of patients with CHD with aspirin, beta-blockers, angiotensin converting enzyme inhibitors (ACEI), or lipid-lowering drugs, separately, lowers the risk of future vascular events by about a quarter each. When used in appropriate combinations they can reduce recurrent vascular events by between two-thirds and three-quarters (7, 8). When the potential benefits of quitting smoking for smokers and of lowering blood pressure in hypertensive patients are added to the four-drug regime, it may be possible to lower the risk of future events in high-risk individuals by more than four-fifths (7, 8).

Although cost-effective treatment is available for the prevention of recurrent vascular attacks, many individuals who have suffered MI or stroke are not receiving adequate preventive treatment even in developed countries (9–15).

There is a scarcity of data related to the secondary prevention of CVD in lower- and middle-income countries, which currently bear 75% of the CVD burden (1). In this context, WHO has initiated a programme on Prevention of REcurrences of Myocardial Infarction and Stroke (WHO-PREMISE) which aims to provide technical cooperation to countries for assessing and scaling up secondary prevention of CVD. Projects have been launched in defined areas in selected countries to assess the current status of secondary prevention (phase 1). The ultimate goal of this programme is to implement evidence-based, affordable and sustainable interventions for secondary prevention, first in the demonstration areas (phase 2) and subsequently on a national scale (phase 3).

Phase 1 of the WHO-PREMISE study is an international multicentre collaborative effort aimed at:

- assessing current practice patterns related to secondary prevention of CHD and CVD;
- documenting the use of secondary prevention interventions; and
- identifying barriers to and opportunities for scaling up secondary prevention.

Methods and data

The WHO-PREMISE study is a descriptive, cross-sectional study involving, at this stage, three low-income and seven middle-income countries (Brazil, Egypt, India, Indonesia, Islamic Republic of Iran, Pakistan, Russian Federation, Sri Lanka,

Tunisia and Turkey). The countries were selected according to the following criteria: logistic feasibility of the study; availability of financial and human resources for its continuation; and commitment of the ministries of health to improving the secondary prevention of CVD.

In each country, one geographical area with a population greater than 500 000 people was selected. A stratified random sample of primary and secondary care facilities was drawn from the catchment area of a randomly identified tertiary care facility in each study area. The sample included private, public, urban and rural facilities.

Selection of patients

One thousand consecutive patients were recruited from the study area in each country over a period of 6 months. Approximately 85% of patients were recruited from the outpatient clinics of secondary and tertiary health care facilities and the remainder from primary health care facilities. The recruitment criteria were: previous MI, stable angina, unstable angina, percutaneous transluminal coronary angioplasty (PTCA), coronary artery bypass graft (CABG), stroke, transient ischaemic attack (TIA) or carotid endarterectomy. Patients were included if their first cardiovascular event had occurred more than 1 month but not later than 3 years ago. The diagnosis was verified by checking the patient's health records. The overall response rate was 80%.

Data collection

During a period of 6 months (in 2002–03), the patients recruited from outpatient clinics were asked to participate in a 30-minute interview. After obtaining informed consent from the patients, interviews were conducted by a trained research assistant using a standardized questionnaire. The following data were collected: demographic and personal details, information on exposure to risk factors, knowledge of and attitude to risk factors, adherence to treatment and perceived barriers, access to care, and availability and affordability of drugs. The presence of diseases and risk factors was recorded based on self-report. The drugs taken were verified by inspecting tablets, past prescriptions, medical records and diagnosis cards.

Training and standardization

The following procedures were used to ensure standardization and high quality of the data: an operations manual; training workshops for national coordinators and research assistants; protocols that described the recruitment criteria, data collection and interview techniques; and detailed notes outlining problems with data collected at specific sites which were compiled and sent periodically to the sites concerned.

Statistical analysis

Forty-three of the 10 000 questionnaires were excluded from the analysis because they were incomplete. We conducted univariate analysis by descriptive statistics of the relevant variables. Means and standard deviations were obtained for quantitative variables; relative frequencies were derived for qualitative variables. Bivariate analysis was applied to categorical data, where appropriate, using a χ^2 test. Multivariate analysis using logistic regression was performed to adjust for potential confounding factors with a 5% significance level. Only variables significant at

Table 2. Logistic regression of significant predictors for medications used by coronary heart disease patients

Predictors	Drug											
	Aspirin			Beta-blockers			ACEIs			Statins		
	Odds ratio	95% CI	P	Odds ratio	95% CI	P	Odds ratio	95% CI	P	Odds ratio	95% CI	P
Age	–	–	–	1.18	1.06–1.31	0.002	0.78	0.70–0.86	< 0.001	1.27	1.10–1.43	0.001
Gender (male)	1.53	1.31–1.79	< 0.001	NS	NS	NS	1.16	1.03–1.30	0.011	1.29	1.11–1.49	0.001
Education	NS	NS	NS	NS	NS	NS				1.19	1.04–1.35	0.009
Payment	NS	NS	NS	1.13	1.01–1.26	0.027	0.78	0.69–0.87	< 0.001			
PTCA + CABG (yes)	NS	NS	NS	NS	NS	NS				2.37	2.07–2.72	< 0.001
Reported HBP (yes)	1.34	1.15–1.57	< 0.001	1.36	1.21–1.52	< 0.001	1.74	1.55–1.95	< 0.001	NS	NS	NS
Reported HBC (yes)	NS	NS	NS	1.20	1.06–1.35	0.004	1.22	1.08–1.38	0.002	4.34	3.77–4.99	< 0.001
Reported HBS (yes)	NS	NS	NS	0.75	0.66–0.86	< 0.001	NS	NS	NS	0.82	0.69–0.98	0.03
Current smoker (yes)	1.83	1.35–2.50	< 0.001	1.32	1.10–1.58	0.002	NS	NS	NS	NS	NS	NS
No. of hospitalizations (> 1)	1.43	1.2–1.66	< 0.001	1.19	1.07–1.32	0.001	1.27	1.14–1.41	< 0.001	NS	NS	NS

CI, confidence intervals; NS, not significant; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft; HBP, high blood pressure; HBC, high blood cholesterol; HBS, high blood sugar.

the 5% bivariate level were included in the multivariate model (see the list of variables in Table 1 (web version only, available at: <http://www.who.int/bulletin>) and Table 2).

Ethical issues

The ethics committee of each study centre sought ethical approval. Informed consent was obtained from each patient prior to participation. All data at the project office were kept secure and anonymous. No subject identifiers appeared on any files transmitted to any committee or any clinical centre.

Results

Baseline characteristics, modes of payment and access to facilities

The mean age of patients in the study was 59.2 years (standard deviation (SD), 10.8). About 45.6% of patients were aged more than 60 years, and 22.5% less than 50 years. These younger patients made up more than 30% of the study population in three of the 10 countries. Table 3 shows the age distribution of patients by country. The majority were men (62.1%). Although women comprised 37.9% of the study sample there was a wide variation between countries in the percentage of women recruited (14.5%–54.5%). The extent to which these data reflect differences in disease prevalence and/or barriers to access to health care is not clear.

About 52% of patients had had secondary education or above, 19% had had primary school education and 29.2% had had no formal education (Table 4, web version only, available at: <http://www.int/bulletin>).

Almost half of the patients (48.7%) paid some or all of the costs of their health care. However, the percentage of patients making full or partial financial contributions varied

widely, ranging from 2.5% to 88.8% in different countries. In no country were health-care services free at the point of use. A primary health care facility was the first point of access for 30.6% (range 10.6–65.9%) of the patients for their most recent cardiovascular event, including for acute MI.

Knowledge of lifestyle-related risk factors and healthy behaviours

Approximately 82%, 89% and 77% of patients were aware of the cardiovascular benefits of quitting smoking, a heart-healthy diet and regular physical activity, respectively. Doctors were the main source of patients' knowledge about lifestyle risk factors. Most patients were aware that they should consume less fat (91.1%), less salt (86.2%) and more fruits (84.7%). Fewer patients (69.9%) were aware of the benefits of consuming fish. About 35% (range 8.2–57.0%) of patients reported difficulties in complying with dietary advice, due mainly to the expense and lack of availability of healthy food items.

In response to questions on their physical activity, 52.5% of study participants reported no engagement in regular moderate physical activity (at least 30 minutes a day). The main reasons reported for inadequate physical activity were: the belief that physical activity has negative effects on health (25.8%), lack of time (10.7%) and lack of facilities (10.9%). A higher percentage of patients with formal education (50%) than uneducated patients (40%) engaged in physical exercise during their leisure time ($\chi^2 = 93.75$; degrees of freedom, 2; $P < 0.001$).

Medications for secondary prevention

Aspirin had been prescribed to 79.6% of CVD patients (range 64.8–94.4%), beta-blockers to 44.2% (range 8.9–69.2%), ACEI to 39.5% (range 10.4–68%) and statins to 19.6% (range

Table 3. Age distribution of patients by country

	Country										Total
	Brazil	Egypt	India	Indonesia	Islamic Rep. of Iran	Pakistan	Sri Lanka	Turkey	Russian Federation	Tunisia	
No. of patients	996	996	1013	999	916	1007	993	1038	999	1000	9957
Mean age (years)											
CHD											
Male	62.7 <i>10.7^a</i>	56.3 <i>8.6</i>	54.6 <i>10.4</i>	57.3 <i>9.1</i>	56.1 <i>11.3</i>	57.5 <i>11.6</i>	60.8 <i>10.3</i>	62.7 <i>10.1</i>	59.3 <i>10.2</i>	62.0 <i>11.2</i>	58.1 <i>10.7</i>
Female	61.6 <i>11.1</i>	53.0 <i>7.6</i>	56.6 <i>10.5</i>	59.0 <i>8.7</i>	59.9 <i>9.6</i>	56.4 <i>10.6</i>	59.4 <i>10.6</i>	62.9 <i>10.3</i>	63.6 <i>10.0</i>	63.2 <i>10.0</i>	59.8 <i>10.6</i>
CVD											
Male	62.1 <i>12.8</i>	59.2 <i>9.6</i>	57.8 <i>8.8</i>	57.5 <i>9.9</i>	64.0 <i>11.3</i>	60.8 <i>8.7</i>	63.8 <i>9.8</i>	65.7 <i>10.2</i>	55.0 <i>7.1</i>	62.0 <i>11.4</i>	60.9 <i>10.9</i>
Female	62.5 <i>14.2</i>	53.6 <i>11.8</i>	52.3 <i>8.8</i>	58.0 <i>11.3</i>	63.2 <i>11.6</i>	56.2 <i>11.8</i>	62.4 <i>9.3</i>	61.3 <i>10.9</i>	58.0 <i>11.5</i>	63.1 <i>10.5</i>	60.7 <i>11.6</i>
Age range (%) (years)											
< 50	15.6	30.3	32.4	22.6	29.7	30.4	16.5	19.1	12.6	15.1	22.5
50–60	26.1	43.7	35.4	40.6	28.8	31.2	29.9	32.4	25.9	25.4	31.9
> 60	58.3	26.0	32.2	36.7	41.5	38.4	53.6	48.4	61.5	59.5	45.6
CHD: male											
< 50	4.4	9.4	22.6	7.8	19.9	14.7	9.8	5.1	4.8	7.9	10.6
50–60	11.1	25.2	32.1	22.2	21.5	21.5	19.4	14.1	12.9	17.7	19.8
> 60	22.3	14.2	24.0	16.2	24.2	23.6	27.2	19.5	26.2	34.4	23.2
Total	37.9	48.8	78.7	46.2	65.6	59.9	56.4	38.6	43.9	60.0	53.5
CHD: female											
< 50	6.5	6.8	3.0	1.6	3.9	6.0	2.4	9.2	3.8	3.5	4.7
50–60	13.4	18.4	5.1	5.2	10.9	10.8	11.2	17.6	8.4	9.3	11.2
> 60	26.2	3.2	5.2	5.1	14.4	8.3	24.8	21.5	22.4	21.3	15.4
Total	46.1	28.4	13.3	11.9	29.3	25.1	38.4	48.3	34.6	34.1	31.3
CVD: male											
< 50	1.1	2.7	1.1	5.1	0.4	0.6	0.4	0.4	0.8	0.7	1.3
50–60	1.9	4.9	3.0	11.2	0.4	3.4	1.9	0.8	2.1	0.5	3.0
>60	4.4	6.8	2.8	9.3	1.4	3.5	0.5	2.7	8.1	2.4	4.2
Total	7.4	14.5	6.8	25.6	2.3	7.4	2.8	3.9	11.0	3.6	8.6
CVD: female											
< 50	1.4	1.9	0.3	3.0	0.1	1.6	0.5	0.3	2.1	0.5	1.4
50–60	1.7	3.5	0.7	5.2	0.5	1.6	1.0	1.1	4.7	0.4	2.4
> 60	5.4	1.4	0.2	4.9	1.2	2.3	1.2	1.7	7.0	1.4	2.8
Total	8.5	6.8	1.2	13.1	1.9	5.5	2.7	3.1	13.8	2.3	6.6

^a Figures in italics are standard deviations.

CHD, coronary heart disease; CVD, cerebrovascular disease.

3.7–39.1%). Among patients with CHD, 18.8 % did not receive aspirin, 51.9% did not receive beta-blockers, 60.2% did not receive ACEI and 79.2% did not receive statins (Table 5).

Measurement and prevalence of cardiovascular risk factors

On average, 94% (range 71–100%) of all CVD patients reported that their blood pressure had been measured within the last 12 months and since the last acute event. The percentage who reported a blood cholesterol check-up ranged from 29% to 97% (mean 86%), and was less than 40% in two countries. The percentage of patients who reported having their blood

sugar measured during the past 12 months was, on average, 76%, and ranged from 65% to 99% across countries.

On average, 12.5% (range 6–19%) of the patients were current smokers. Past smokers constituted 26.8% of the total study population, but there was great variability between countries (range 4%–48%). On average, 67.7% of patients reported high blood pressure and 40.3% high levels of blood cholesterol. About one-third (31.5%) of patients reported that they had diabetes. Analysis of the extent of exposure to risk factors, found that an average of only 16.2% of patients had no major coronary risk factors. About 46.6% of patients were exposed to at least two risk factors, and 16.4% at least three.

Table 5. Use of medications in patients with coronary heart disease and cerebrovascular disease by country

	Country										Total
	Brazil	Egypt	India	Indonesia	Islamic Rep. of Iran	Pakistan	Sri Lanka	Turkey	Russian Federation	Tunisia	
<i>n</i>	996	996	1013	999	916	1007	993	1038	999	1000	9957
Use of medications in patients with CHD											
No. of patients	836	776	932	596	877	874	918	789	944	941	8483
Aspirin (%)	65.9	82.7	94.5	78.7	81.3	96.1	66.3	78.2	88.7	77.6	81.2
Beta-blockers (%)	45.2	35.2	46.2	34.2	66.0	60.5	8.7	45.6	72.2	59.6	48.1
ACEI (%)	53.0	22.6	41.3	45.3	27.9	45.1	10.8	40.2	69.6	41.6	39.8
Statins (%)	28.6	8.6	38.4	30.9	28.1	15.6	3.81	23.1	27.5	5.84	20.8
Use of medications in patients with cerebrovascular (CVD) disease											
No. of patients	160	212	81	403	39	133	75	249	55	59	1466
Aspirin (%)	58.8	78.8	90.1	72.2	43.6	83.5	62.7	69.5	30.9	72.9	70.5
Beta-blockers (%)	33.1	29.7	28.4	7.4	46.2	35.3	10.7	27.7	16.4	6.8	22.1
ACEI (%)	44.4	22.6	23.5	58.8	10.3	43.6	5.3	35.7	40.0	10.2	38.1
Statins (%)	16.9	11.8	37.0	12.9	12.8	2.3	2.7	10.0	16.4	1.7	12.2

CHD, coronary heart disease; CVD, cerebrovascular disease; ACEI, angiotensin converting enzyme inhibitors.

Sociodemographic and clinical characteristics and use of medication

Table 1 (web version only, available at: <http://www.int/bulletin>) summarizes the bivariate association between the use of medications and the sociodemographic and clinical parameters of all CVD patients. Higher reported number of hospitalizations, high blood cholesterol and high blood pressure were associated with increased use of most or all medications. Use of statins was particularly associated with being male, younger age, higher educational attainment and revascularization. Mode of payment (free versus part or full payment) was not associated with statin use, but free treatment was associated with increased use of aspirin and reduced use of ACEIs.

Table 2 presents a multivariate analysis of predictors for the use of each medication among patients with CHD, after adjusting for potential confounding factors. The most significant predictors were as follows:

- *of aspirin use*: current smoking (odds ratio (OR), 1.83; 95% CI, 1.35–2.50) and male gender (OR, 1.53; 95% CI, 1.31–1.79);
- *of beta blocker use*: reported high blood pressure (OR, 1.36; 95% CI, 1.21–1.52) and current smoking (OR, 1.32; 95% CI, 1.10–1.58);
- *of ACE inhibitor use*: reported high blood pressure (OR, 1.74; 95% CI, 1.55–1.95) and male gender (OR, 1.16; 95% CI, 1.03–1.30);
- *of statin use*: reported high blood cholesterol (OR, 4.34; 95% CI, 3.77–4.99), PTCA or CABG surgery (OR, 2.37; 95% CI, 2.07–2.72) and male gender (OR, 1.29; 95% CI, 1.11–1.49).

Discussion

This study was conducted to gain an overview of the situation and identify barriers to secondary prevention of CVD in low-

and middle-income countries. However the results of the study should be interpreted with caution. It should be recognized that the study has some limitations in terms of its generalizability. The data do not represent national profiles and therefore should not be used for comparisons between different countries. Sampling of patients from health-care facilities introduces a selection bias. Patients who attend outpatient clinics are likely to differ from the general population with regard to their health-seeking behaviour and access to health services. Also, in our study, the patients recruited from primary care facilities constituted only 15% of the sample. The situation regarding secondary prevention of CVD in the general population and among patients who attend primary care facilities is likely to be far worse than in our sample. Despite these limitations the study provides a useful insight into current practice with regard to secondary prevention.

We are also aware that the design and performance of health systems in various countries might be partly responsible for the differences in secondary prevention of CVD that we found, and health system-specific variables for each country were not included in the multivariate analysis.

Another limitation of this study is that the CVD risk factor profiles were based on patient self-reports which may have questionable validity and may be affected by cultural differences between populations. We tried to minimize the potential biases by using standardized data collection procedures and training of interviewers.

A resource-intensive population-based coverage study is required to address some of these limitations and will be conducted at the same sites in the future.

There is robust scientific evidence for recommending the use of aspirin (16), lipid lowering agents (17–19), beta-blockers (20) and ACEI (21) for the secondary prevention of CVD. Recent data from studies in Europe and the USA suggest

that there are significant gaps in secondary prevention even in developed countries (22–24). For example, a US study based on national registry data, EUROASPIRE II (European Action on Secondary Prevention by Intervention to Reduce Events) and other European studies have reported suboptimal prescription rates in patients with established CHD (22, 25, 26). Our results corroborate those of EUROASPIRE I and II with respect to the use of aspirin in CHD patients (81.2% in our study compared to 83.9% in EUROASPIRE II (25) and 81% for EUROASPIRE I (23)). The low cost of aspirin and its almost universal availability may explain the similarity of the findings.

The use of beta-blockers, however, was lower in the PREMISE study than in EUROASPIRE II (51.9% versus 66.4%). The use of ACEI in the PREMISE study was quite similar to that reported by EUROASPIRE II (38.8% and 42.7%, respectively). For statins we observed a very low rate of use, 20.8% as opposed to 57.7% reported by EUROASPIRE II. It is of concern that about one-tenth of patients with coronary heart disease in the PREMISE study were not on any medications, not even on aspirin or beta-blockers which are inexpensive and widely available.

The treatment gaps observed in the PREMISE study could have several causes, such as lack of implementation of evidence-based clinical practice by health-care providers; unaffordability and unavailability of medications; and selective prescription of drugs to certain categories of patients, among others (27).

In the PREMISE study 24.5%, 14.5% and 6.2% of patients, respectively, had not had their blood sugar, blood cholesterol and blood pressure checked in the past year. Lack of facilities in health-care centres, the need for patients to pay for tests and differences in health care practice may have contributed to these deficiencies.

In our study, fewer patients reported being smokers (12.5%) than recorded in EUROASPIRE II (21%). Although the potential effects of selection and information bias cannot be ruled out, this might be related to a generally lower prevalence of smoking in the populations of some of the countries participating in the PREMISE study (28). Furthermore the smoking prevalences in the present study were not adjusted for gender and age, and are therefore difficult to compare within our study across countries, and across different studies.

Drug treatment is by no means the only effective method of secondary prevention. Dietary advice, smoking cessation, weight reduction, physical exercise and other non-pharmacological preventive interventions are crucial for improving the cardiovascular risk profile and prognosis of patients with CVD (29–32). In our study nearly 84% of patients had risk factors. These findings are in agreement with those of Khot et al. (33) who reported the presence of one or more conventional risk factors in 80.6% of patients with CHD enrolled in 14 international clinical trials.

About a quarter of the patients with CVD held the erroneous belief that they should not engage in physical activity and a significant proportion lacked knowledge and awareness of major lifestyle risks although they were cared for by physicians. If health-care providers do not miss opportunities for patient health education and counselling, this can have a significant positive effect on smoking cessation, patients' dietary habits and physical activity. It is also important to note that a substantial proportion of patients had had no formal education (29.2%), highlighting the need for simple health education messages and methods of communication.

The findings of our study also point to a clear need for capacity building in health care systems in low- and middle-income countries both in terms of infrastructure and human resources. Bearing in mind that in the PREMISE study about one-third of patients accessed primary health care facilities for obtaining treatment, primary health care physicians need to be targeted in continuing medical education programmes related to secondary prevention and should be provided with suitable incentives to engage in clinical prevention. There is considerable potential for improving secondary prevention of CVD through better clinical prevention, particularly in primary health care (34). Repeated advice by health-care professionals to stop smoking is of great importance. Physicians should recognize the importance of documenting smoking status, body mass index and the level of physical activity during follow-up visits (35, 36).

In conclusion, despite the availability of cost-effective interventions, there are significant gaps in secondary prevention of CVD in low- and middle-income countries. There is a need to increase access to preventive drug therapy and to improve the quality of provider–patient relationships. This would ensure that patients benefit fully from available knowledge and medical technology in the secondary prevention of CVD. Health system capacity for managing CVD needs to be enhanced through the development of effective national drug policies, rational and evidence-based selection of medicines for inclusion in national drug lists, affordable prices for pharmaceuticals and sustainable financing and supply systems. Proactive policies are also required to promote clinical prevention, strengthen the infrastructure of health-care facilities particularly at the primary health care level, and to provide continuing medical education to health-care providers. To ensure sustainability of these measures, they need to be supported with complementary population-wide strategies that promote healthy lifestyles. Finally effective information systems are crucial for monitoring the performance of secondary prevention programmes. ■

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Résumé

Étude OMS sur la prévention des récurrences d'infarctus du myocarde et d'accident vasculaire cérébral (WHO-PREMISE)

Objectif Déterminer l'ampleur de la prévention secondaire des cardiopathies coronariennes et des accidents vasculaires cérébraux (AVC) dans les pays à revenus faibles et moyens.

Méthodes Une étude descriptive transversale d'un échantillon comprenant 10 000 cas d'AVC (85,2 %) et de cardiopathies coronariennes (14,8 %) et composé de 6252 hommes et 3748 femmes a été menée sur 6 mois dans des zones définies géographiquement. L'âge moyen des malades était de 59,2 ans (écart type : 10,8). Les malades ont été successivement recrutés à partir d'un échantillon stratifié d'installations de soins de santé primaires, secondaires et tertiaires, situées dans des zones définies de 10 pays (Brésil, Égypte, Inde, Indonésie, République Islamique d'Iran, Pakistan, Fédération de Russie, Sri Lanka, Tunisie et Turquie). Les principaux critères d'évaluation utilisés étaient le mode de vie, les facteurs de risque physiologiques et l'utilisation de médicaments pour la prévention secondaire des cardiopathies coronariennes et des AVC.

Résultats Environ 82 %, 89 % et 77 % respectivement des malades étaient conscients des bénéfices sur le plan cardiovasculaire d'un arrêt du tabac, d'un régime alimentaire sain pour le cœur et d'une activité physique régulière. Environ la moitié (52,5 %)

avaient pratiqué moins de 30 min d'activité physique par jour, 35 % n'avaient pas suivi de régime sain pour le cœur et 12,5 % étaient encore consommateurs de tabac. Au cours des 12 mois précédents, on avait mesuré la tension artérielle chez 93,8 % en moyenne (71 à 100 % des sujets), le taux de cholestérol sanguin chez 85,5 % en moyenne (29 à 97 %) des sujets et le taux de sucre dans le sang chez 75,5 % en moyenne (65 à 99 %) d'entre eux. Parmi les personnes ayant souffert d'un AVC ou d'une cardiopathie coronarienne, 81,2 et 70,6 % respectivement avaient reçu de l'aspirine, 48,1 et 22,8 % respectivement, des bêta-bloquants, 39,8 et 37,8 % respectivement, de l'inhibiteur de l'enzyme de conversion et 29,8 et 14,1 % respectivement, des statines. Environ un cinquième des personnes victimes d'un AVC avaient subi une revascularisation.

Conclusion Une proportion importante des malades n'avait pas reçu de médication appropriée. Environ 47 % d'entre eux présentaient au moins deux facteurs de risque ou plus modifiables (tabagisme, inactivité physique, hypertension, diabète ou hypercholestérolémie). Dans les pays à revenus faibles et moyens, les possibilités non exploitées de prévenir les récurrences chez les personnes ayant subi un AVC sont donc considérables.

Resumen

Estudio de la OMS sobre la prevención de las recidivas de infarto de miocardio y de accidente cerebrovascular (WHO-PREMISE)

Objetivo Determinar el grado de prevención secundaria de la cardiopatía coronaria (CC) y las enfermedades cerebrovasculares (ECV) en los países de ingresos bajos y medios.

Métodos A lo largo de 6 meses se llevó a cabo un estudio transversal descriptivo de una muestra de 10 000 casos de CC (85,2%) y de ECV (14,8%) (6252 hombres; 3748 mujeres) en varias zonas geográficas delimitadas. La media de edad era de 59,2 años (desviación estándar: 10,8). Se seleccionó a pacientes consecutivos en una muestra aleatoria estratificada de establecimientos de atención primaria, secundaria y terciaria de zonas concretas de 10 países (Brasil, Egipto, India, Indonesia, República Islámica del Irán, Pakistán, Federación de Rusia, Sri Lanka, Túnez y Turquía). Las principales medidas de resultado fueron los niveles de diversos factores de riesgo fisiológicos o relacionados con el modo de vida, y el uso de medicamentos de prevención secundaria de la CC y la ECV.

Resultados Aproximadamente el 82%, el 89% y el 77% de los pacientes conocían los beneficios cardiovasculares que conllevan dejar de fumar, una dieta cardiosaludable y la actividad física regular, respectivamente. Alrededor de la mitad (52,5%) hacían

menos de 30 minutos de actividad física al día, el 35% no seguía una dieta cardiosaludable, y el 12,5% eran fumadores habituales en el momento del estudio. La tensión arterial había sido determinada en un 93,8% de los casos (intervalo: 71%–100%), el colesterol sanguíneo en un 85,5% (intervalo: 29%–97%) y la glucemia en un 75,5% (intervalo 65%–99%) durante los 12 meses precedentes. El porcentaje de pacientes que habían recibido medicamentos entre quienes habían sufrido CC y ECV fueron los siguientes: aspirina, 81,2% y 70,6%; betabloqueantes, 48,1% y 22,8%; inhibidores de la enzima convertidora de la angiotensina, 39,8% y 37,8%; y estatinas, 29,8% y 14,1%, respectivamente. Alrededor de una quinta parte de los pacientes con CC habían sido sometidos a revascularización.

Conclusión Una proporción considerable de los pacientes no recibía la medicación adecuada. Alrededor del 47% de los enfermos presentaban dos o más factores de riesgo modificables (tabaquismo, inactividad física, hipertensión, diabetes o hipercolesterolemia). Se están desaprovechando muchas oportunidades para prevenir las recidivas en las personas que han sufrido un accidente cerebrovascular en los países de ingresos bajos y medios.

Arabic

References

1. The World Health Report 2002. Reducing risks, promoting healthy life. Geneva: World Health Organization; 2002.
2. Chambless L, Keil U, Dobson A, Mahonen M, Kuulasmaa K, Rajakangas AM, et al. Population versus clinical view of case fatality from acute coronary heart disease: results from the WHO MONICA Project 1985–1990. Multinational MONItoring of Trends and Determinants in Cardiovascular Disease. *Circulation* 1997;96:3849-59.
3. Mehta RH, Eagle KA. Secondary prevention in acute myocardial infarction. *BMJ* 1998;316:838-42.
4. Royal College of Surgeons. National clinical guidelines for stroke. London: Royal College of Surgeons; 2000.
5. Law MR, Watt HC, Wald NJ. The underlying risk of death after myocardial infarction in the absence of treatment. *Arch Int Med* 2002;162:2405-10.
6. Secondary prevention of noncommunicable diseases in low- and middle-income countries through community-based and health service interventions. Geneva: World Health Organization; 2002. WHO document WHO/EDM/2000.1. World Health Organization – Wellcome Trust meeting report, 1–3 August 2001.
7. Yusuf S. Two decades of progress in preventing vascular disease. *Lancet* 2002;360:2-3.
8. Wald NJ, Law MR. A strategy to reduce cardiovascular disease by more than 80%. *BMJ* 2003;326:1419.
9. McCormick D, Gurwitz JH, Lessard D, Yarzebski J, Gore JM, Goldberg RJ. Use of aspirin, β -blockers, and lipid-lowering medications before recurrent acute myocardial infarction. *Arch Int Med* 1999;159:561-67.
10. Campbell NC, Thain J, Deans HG, Ritchie LD, Rawles JM. Secondary prevention in coronary heart disease. *BMJ* 1998;316:1430-34.
11. Ellerbeck EF, Jencks SF, Radford MJ, Kresowik TF, Craig AS, Gold JA, et al. Quality of care for Medicare patients with acute myocardial infarction. *JAMA* 1995;273:1509-14.
12. The Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *NEJM* 2000;342:145-53.
13. Schwartz GG, Olsson AG, Ezekowitz MD, Ganz P, Oliver MF, Waters D, et al. Effects of atorvastatin on early recurrent ischemic events in acute coronary syndromes. *JAMA* 2001;285:1711-8.
14. Sacks FM, Pfeffer MA, Moyer LA, Rouleau JL, Rutherford JD, Cole TG, et al. The effect of pravastatin on coronary events after myocardial infarction in patients with average cholesterol levels. *NEJM* 1996;335:1001-9.
15. Pitt B, Byington RP, Furberg CD, Hunninghake DB, Mancini GB, Miller ME, et al. Effect of amlodipine on the progression of atherosclerosis and the occurrence of clinical events. *Circulation* 2000;102:1503-10.
16. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;324:71–86.
17. Aronow HD, Topol EJ, Roe MT, Houghtaling PL, Wolski KE, Lincoff AM, et al. Effect of lipid-lowering therapy on early mortality after acute coronary syndromes: an observational study. *Lancet* 2001;357:1063-8.
18. Bucher HC, Griffith LE, Guyatt GH. Systematic review on the risk and benefit of different cholesterol lowering interventions. *Arterioscler Thromb Vasc Biol* 1999;19:187-95.
19. Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. *BMJ* 2003;326:1423-9.
20. Freemantle N, Cleland J, Young P, Mason J, Harrison J. Beta blockade after myocardial infarction: systematic review and meta regression analysis. *BMJ* 1999;318:1730-7.
21. Pfeffer MA, Braunwald E, Moyer LA, Basta L, Brown EJ Jr, Cuddy TE, et al. Effect of captopril on mortality and morbidity in patients with left ventricular dysfunction after myocardial infarction. Results of the survival and ventricular enlargement trial. The SAVE Investigators. *NEJM* 1992;327:669-77.
22. Fonarow GC, French WJ, Parsons LS, Sun H, Malmgren JA. Use of lipid lowering medications at discharge in patients with acute myocardial infarction: data from the National Registry of Myocardial Infarction 3. *Circulation* 2001;103:38-44.
23. EUROASPIRE Study Group. A European Society of Cardiology survey on secondary prevention of coronary heart disease. Principal results. *Eur Heart J* 1997;18:1569-82.
24. EUROASPIRE II Group. Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries: principal results from EUROASPIRE II Euro Heart Survey Programme. *Eur Heart J* 2001;22:554-72.

25. EUROASPIRE I and II Group. Clinical reality of coronary prevention guidelines: a comparison of EUROASPIRE I and II in nine countries. *Lancet* 2001; 357:995-1001.
26. Steg PG, Lung B, Feldman LJ, Cokkinos D, Deckers J, Fox KA, et al. Impact of availability and use of coronary interventions on the prescription of aspirin and lipid lowering treatment after acute coronary syndromes. *Heart* 2002; 88:20-4.
27. Reid FDA, Cook DG, Whincup PH. Use of statins in the secondary prevention of coronary heart disease: is treatment equitable? *Heart* 2002;88:15-9.
28. Ahmadi J, Khalili H, Jooybar R, Namazi N, Mohammadagaei P. Prevalence of cigarette smoking in Iran. *Psychol Rep* 2001;89:339-41.
29. Kromhout D, Menotti A, Kesteloot H, Sans S. Prevention of coronary heart disease by diet and lifestyle: Evidence from prospective cross cultural, cohort and intervention studies. *Circulation* 2002;105:893-8.
30. Hjermann I, Velve Byre K, Holme I, Leren P. Effect of diet and smoking intervention on the incidence of coronary heart disease. Report from the Oslo Study Group of a randomised trial in healthy men. *Lancet* 1981;2:1303-10.
31. De Lorgeril M, Salen P, Martin JL, Monjaud I, Delaye J, Mamelle N. Mediterranean diet, traditional risk factors, and the rate of cardiovascular complications after myocardial infarction: final report of the Lyon Diet Heart Study. *Circulation* 1999;99:779-85.
32. Ornish D, Scherwitz LW, Billings JH, Brown SE, Gould KL, Merritt TA, et al. Intensive lifestyle changes for reversal of coronary heart disease. *JAMA* 1998; 280:2001-7.
33. Khot UN, Khot MB, Bajzer CT, Sapp SK, Ohman EM, Brener SJ, et al. Prevalence of conventional risk factors in patients with coronary heart disease. *JAMA* 2003;290:898-904.
34. Hobbs FD, Erhardt L. Acceptance of guideline recommendations and perceived implementation of coronary heart disease prevention among primary care physicians in five European countries: the Reassessing European Attitudes about Cardiovascular Treatment (REACT) survey. *Fam Prac* 2002;19:596-604.
35. Van Berkel TF, Boersma H, De Baquer D, Deckers JW, Wood D. Registration and management of smoking behaviour in patients with coronary heart disease. The EUROASPIRE survey. *Eur Heart J* 1999;20:1630-7.
36. Montaye M, De Bacquer D, De Backer G, Amouyel P. Overweight and obesity: a major challenge for coronary heart disease secondary prevention in clinical practice in Europe. *Eur Heart J* 2000;21:808-13.

Table 1. Use of medications *n* (%) by sociodemographic and clinical characteristics and reported cardiovascular risk factors among all patients with cardiovascular disease

	Aspirin	Beta-blockers	ACEI	Statins
Gender				
Male	5876 (86.7) ^a	5417 (53.5)	5358 (47.7)	5243 (26)
Female	3315 (82.9)	2868 (51.4)	2832 (47.4)	2733 (20.7)
<i>P</i>	< 0.001	NS	NS	< 0.001
Age (years)				
≤ 60	5116 (85.4)	4601 (53.8)	4543 (45.4)	4446 (26.4)
> 60	4162 (85.4)	3752 (51.3)	3717 (50.3)	3599 (21.4)
<i>P</i>	NS	NS	< 0.001	< 0.001
Education				
Up to primary	4479 (84.8)	4214 (53.2)	4166 (46.5)	4049 (21.7)
Secondary and above	4656 (85.8)	4031 (52.3)	3989 (49)	3893 (26.8)
<i>P</i>	NS	NS	NS	< 0.001
Mode of payment				
Free	4061 (86.9)	3313 (52.3)	3284 (51.6)	3130 (25)
In part or in full	5130 (84.1)	4958 (53)	4894 (56.6)	4834 (23.7)
<i>P</i>	0.001	NS	< 0.001	NS
Diagnosis category				
PTCA + CABG	2055 (86.9)	1956 (56.4)	1881 (46.4)	1876 (40.9)
Other CHD	5847 (87.3)	5132 (57.9)	5111 (48.9)	4934 (20.2)
<i>P</i>	NS	NS	NS	<0.001
Reported high blood pressure				
Yes	6257 (86.6)	5547 (54.9)	5525 (53.6)	5287 (24.1)
No	2993 (82.8)	2783 (48.3)	2714 (35.5)	2736 (24.3)
<i>P</i>	< 0.001	< 0.001	< 0.001	NS
Reported high blood cholesterol				
Yes	3457 (86.1)	3269 (55.9)	3213 (50.7)	3178 (40.2)
No	5312 (84.4)	4643 (49.8)	4623 (45.9)	4453 (13.8)
<i>P</i>	NS	< 0.001	0.001	<0.001
Reported high blood sugar				
Yes	3099 (87.4)	2863 (50.8)	2836 (47.9)	2778 (25.4)
No	6121 (84.4)	5443 (53.6)	5380 (47.6)	5220 (23.5)
<i>P</i>	0.001	NS	NS	NS
Current smoker				
Yes	1082 (89.2)	984 (58.5)	974 (48.8)	936 (22.3)
No	7973 (84.9)	7203 (51.8)	7128 (47.6)	6957 (24.3)
<i>P</i>	0.001	0.001	NS	NS
Number of hospitalizations				
≤ 1	5008 (83.1)	4546 (48.7)	4519 (45.4)	4402 (20.9)
> 1	4270 (88)	3807 (57.5)	3741 (50.4)	3643 (28.1)
<i>P</i>	< 0.001	< 0.001	< 0.001	< 0.001
Number of risk factors				
≤ 2	7121 (83.4)	7115 (51.7)	7028 (46.5)	6840 (22.5)
> 2	1245 (88.8)	1238 (52.7)	1232 (54.1)	1205 (33.4)
<i>P</i>	< 0.001	NS	< 0.001	< 0.001

^a Figures in parentheses are percentages.

ACEI, Angiotensin converting enzyme inhibitors; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft.

Table 4. Baseline characteristics of patients by country

	Country										Total
	Brazil	Egypt	India	Indonesia	Islamic Rep. of Iran	Pakistan	Sri Lanka	Turkey	Russian Federation	Tunisia	
Gender (%)											
CHD											
Male	37.9	48.8	78.7	46.2	65.6	59.9	56.4	38.6	43.9	60.0	53.5
Female	46.1	28.4	13.3	11.9	29.3	25.1	38.4	48.3	34.6	34.1	31.0
CVD (%)											
Male	7.4	14.5	6.8	25.6	2.3	7.4	2.8	3.9	11.0	3.6	8.6
Female	8.5	6.8	1.2	13.1	1.9	5.5	2.7	3.1	13.8	2.3	5.9
Diagnosis category (%)											
CHD	43.3	72.3	50.0	33.9	55.2	84.7	92.2	37.9	88.9	81.9	64
PTCA or CABG	40.7	5.6	42.0	25.7	40.5	2.1	0.2	38.2	5.6	12.2	21.2
CVD	16.1	21.3	8.0	40.3	4.3	13.2	7.6	24.0	5.5	5.9	14.8
Level of education (%)											
No formal education	12	37	15	40	38	45	7	16	32	51	29.2
Primary	8	25	29	2	15	26	5	58	2	20	19
Secondary and above	80	38	56	58	47	29	88	26	66	29	51.8
Mode of payment (%)											
Free	93.5	49.1	63.8	16.6	11.2	24.6	97.5	96.3	38.6	15.9	51.3
Part payment	4.3	44.9	23.3	43.7	81	60.5	1.3	2.4	51.6	81.1	38.9
Full payment	2.2	7	12.9	39.7	7.8	14.9	1.2	1.3	9.8	3	9.8
Facility first accessed (%)											
Primary care	33.5	34.8	47.0	21.8	17.7	21.6	27.4	10.6	65.9	25.2	30.6
Secondary care	33.1	38.9	25.4	43.5	59.0	3.6	68.0	54.8	27.1	24	37.9
Tertiary care	33.3	26.3	27.6	34.6	23.4	74.8	4.7	34.6	5.1	50.8	31.5

CHD, coronary heart disease; CVD, cerebrovascular disease; PTCA, percutaneous transluminal coronary angioplasty; CABG, coronary artery bypass graft.

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