

# Continuously improving the practice of cardiology

M.L. Simoons, M.J. de Boer, E. Boersma, H.J.G.M. Crijns, J.W. Deckers, J. Funke Küpper, M. Lenzen, K.I. Lie, H.R. Michels, R. Nieuwlaat, J.P. Ottervanger, P. Polak, W. Scholte op Reimer, E. de Swart, F. Vermeer, E.E. van der Wall

Guidelines for the management of patients with cardiovascular disease are designed to assist cardiologists and other physicians in their practice. Surveys are conducted to assess whether guidelines are followed in practice. The results of surveys on acute coronary syndromes, coronary revascularisation, secondary prevention, valvular heart disease and heart failure are presented. Comparing surveys conducted between 1995 and 2002, a gradual improvement in use of secondary preventive therapy is observed. Nevertheless, important deviations from established guidelines are noted, with a significant variation among different hospitals in the Netherlands and in other European countries. Measures for further improvement of clinical practice include more rapid treatment of patients with evolving myocardial infarction, more frequent use of clopidogrel and glycoprotein IIb/IIIa receptor blockers in patients with acute coronary syndromes, more frequent use of  $\beta$ -blockers in patients with heart failure and more intense measures to encourage patients to stop smoking. Targets for the proportion of patients who might receive specific therapies are presented. (*Neth Heart J* 2004;12:110-6.)

Key words: acute coronary syndromes, PCI, CABG, prevention, heart failure, checklist, guidelines, thrombolysis

---

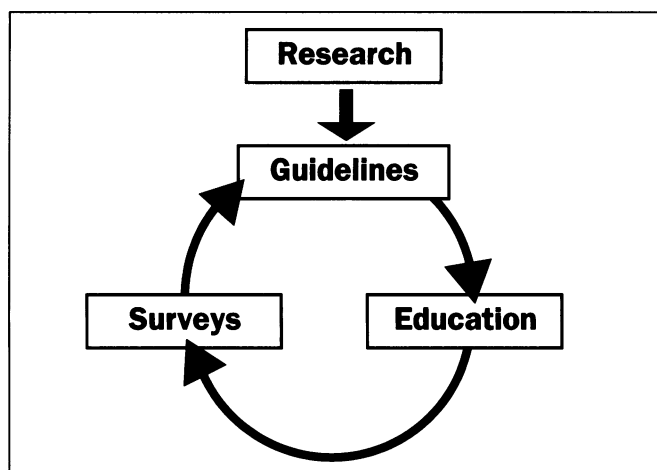
**Workgroup of the Netherlands Heart Foundation**  
M.L. Simoons, M.J. de Boer, E. Boersma, H.J.G.M. Crijns,  
J.W. Deckers, J. Funke Küpper, M. Lenzen, K.I. Lie,  
H.R. Michels, R. Nieuwlaat, J.P. Ottervanger, P. Polak,  
W. Scholte op Reimer, E. de Swart, F. Vermeer,  
E.E. van der Wall  
Erasmus Medical Center - Thoraxcenter, Dr. Molewaterplein 40,  
3015 GD Rotterdam

Correspondence to: M.L. Simoons  
E-mail: m.simoons@erasmusmc.nl

**O**ur tools for prevention, detection, diagnosis and treatment of cardiovascular disease have markedly improved in the last decades, and continue to improve. For example, we notice a rapid evolution in the use of biochemical markers for inflammation, thrombosis, atherosclerosis and heart failure in addition to classical risk factors, as well as improved and new imaging modalities (echocardiography, MRI, multislice CT). Furthermore, interventional cardiology is developing rapidly, both for coronary interventions as well as for correction of congenital and other structural heart diseases, clinical electrophysiology, devices for treatment of arrhythmias and cardiothoracic surgery. Moreover, there is a rapid evolution in drug therapy for prevention and management of atherosclerosis, arrhythmias, hypertension, diabetes and heart failure. The evidence for the efficacy of new, improved therapies is often based on large-scale clinical trials.

To assist the cardiologists in clinical decision-making in this rapidly evolving field, guidelines are established for prevention, detection and management of cardiovascular disease. These guidelines combine pathophysiological insight, evidence from clinical trials as well as the evolution of clinical experience as judged by panels of experts. Cardiologists as well as other physicians are encouraged to apply these guidelines in their practice (figure 1). However, it is also appreciated that management of individual patients is more complex than simply following the available guidelines. Individual patient characteristics may require a personalised approach, while application of guidelines may also be hampered by (lack of) facilities or waiting lists.

To assess whether guidelines are being followed in clinical practice, and whether patients in actual practice are properly reflected by the clinical trials on which guidelines are often based, the Euro Heart Survey programme and the 'Zorgprogramma of the Netherlands Heart Foundation' have been developed. At the autumn meeting of the Netherlands Society of

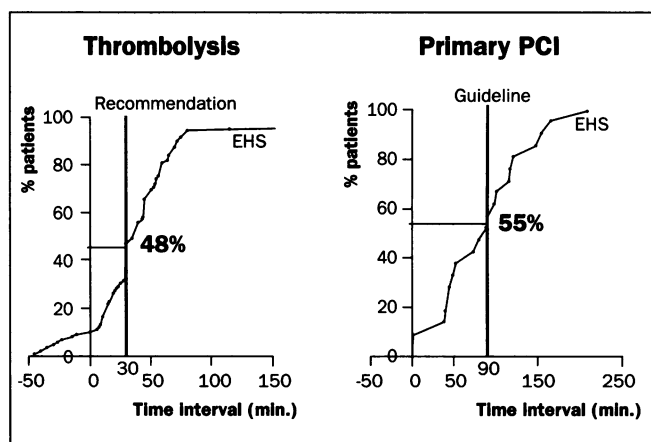


*Figure 1. Guidelines reflect the state of the art of clinical practice, based on findings from clinical and experimental research. Education programmes (in the Netherlands CVOI) should reflect the guidelines. Surveys of the actual practice provide information about guideline adherence, and may result in adaptation of the guidelines as well as improved education programmes.*

Cardiology on 24 October 2003, the results of the Euro Heart Survey/Zorgprogramma were presented and discussed. Guideline-based checklists were proposed, which may assist cardiologists as well as other physicians to systematically record different aspects of patient care. Finally, recommendations on the proportion of patients requiring specific therapies have been formulated by members of the Committee for the Euro Heart Survey/Zorgprogramma in the Netherlands, and the Committee for Quality Assurance (Commissie Kwaliteit) of the Netherlands Society of Cardiology. A summary of the recommendations is presented in this report.

#### Acute coronary syndromes with ST elevation

In patients with evolving myocardial infarction (ACS with ST elevation), reperfusion therapy is indicated if there is a history of symptoms starting within 12 hours of presentation, with ST-segment elevation or presumed new bundle branch block. The preferred therapy is primary percutaneous coronary intervention (PCI), if this can be performed by an experienced team within 90 minutes after first medical contact. The alternative treatment is thrombolysis, as soon as possible, when contraindications are absent and primary PCI cannot be performed timely by an experienced team.<sup>1</sup> In the Euro Heart Survey Acute Coronary Syndromes, conducted in 2000 and 2001, 4431 patients with ST elevation or new bundle branch block were registered. In the Netherlands, primary PCI was offered in 11%, thrombolysis in 54%, and 35% did not receive early reperfusion therapy.<sup>2</sup> Furthermore, it was apparent that in about half of the patients the time interval between arrival in hospital and reperfusion therapy exceeded the recommendations (figure 2). In 52% of patients



*Figure 2. Time interval between arrival in emergency department ( $t=0$ ) and initiation of thrombolytic therapy (left panel) or first balloon inflation (right panel). Guidelines specify initiation of thrombolytic therapy early, within 30 minutes after hospital arrival. This is achieved in 48% of patients. Primary PCI should be conducted within 90 minutes after hospital arrival, which is achieved in 55% of patients.*

registered in the Netherlands it took more than 30 minutes after hospital arrival before thrombolytic therapy was started, while in 45% of those referred for primary PCI, the treatment delay in hospital was more than 90 minutes. About 10% of patients received prehospital thrombolytic therapy.

To optimise patient management it is recommended that every hospital or region develops a protocol for patients with evolving myocardial infarction, taking into account the local infrastructure. Main objectives should be to offer reperfusion therapy to all patients presenting within 12 hours after symptom onset, with ST elevation or a presumed new left bundle branch block. If primary PCI is offered, at least 75% of patients should be treated within 90 minutes (time from hospital arrival to first balloon inflation). In patients treated with thrombolysis the infusion should be started within 30 minutes after hospital arrival in at least 75% of patients. The checklist presented in table 1 may be used to register your hospital's performance.

**Table 1.** Checklist emergency care ACS.

- ST elevation or new LBBB?	Y / N
- Time onset symptoms	
- ER < 12 hours	Y / N
- Reperfusion therapy	Y / N
Why not?	.....
- Primary PCI, reason for choice	.....
Time interval: ER – primary PCI	time:
- Thrombolysis, reason for choice	.....
Time interval: ER – thrombolysis	time:

**Table 2.** In-hospital medical therapy (EHS-NL).

ST elevation	Observed	Target
Aspirin	93%	>90%
Beta-blocker (iv/orally)	86%	>75%
GP IIb/IIIa + primary PCI	72%	>90%
LMWH + thrombolysis	15%	>90%

In patients with evolving myocardial infarction (ACS with ST elevation) aspirin and  $\beta$ -blockers are recommended. Guidelines recommend glycoprotein IIb/IIIa receptor blockers for all patients undergoing primary PCI, or a combination of a fibrinolytic agent with low-molecular-weight heparin in case of thrombolysis. Table 2 presents the recommended (target) and observed use of these agents in the Euro Heart Survey in the Netherlands. Indeed, aspirin and  $\beta$ -blockers are used as expected, while the use of glycoprotein IIb/IIIa receptor blockers and low-molecular-weight heparin is less than expected. This may be an issue of costs and limited healthcare resources.

**Acute coronary syndromes without ST-segment elevation**

Management of patients with ACS without ST elevation is recommended to include aspirin, combined with clopidogrel, heparin (unfractionated or low-molecular-weight) as well as a  $\beta$ -blocker. Coronary angiography is recommended in patients at increased risk of death or myocardial infarction.<sup>3,4</sup> Severe risk scores have been proposed to identify patients requiring angioplasty and revascularisation. In patients undergoing PCI for acute coronary syndromes, GP IIb/IIIa receptor blockers are recommended in the guidelines. It should be appreciated, however, that the opinion of the cardiologists present at the autumn meeting of the Netherlands Society of Cardiology deviated from this recommendation. About equal proportions indicated that GP IIb/IIIa receptor blockers should be used in about 50%, in at least 75% or in almost all

**Table 4.** Checklist in-hospital medical therapy.

All ACS patients:	Prescribed	If no, why not:
Aspirin	Y / N	.....
Beta-blocker	Y / N	.....
Non-ST $\uparrow$ ACS:		
Clopidogrel	Y / N	.....
Heparin	Y / N	.....
UFH	Y / N	.....
LMWH	Y / N	.....
PCI : GP IIb/IIIa	Y / N	.....

**Table 3.** In-hospital medical therapy (EHS-NL).

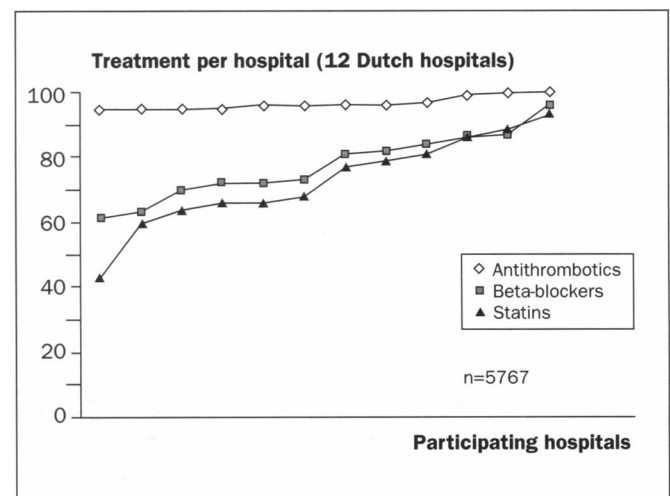
Non-ST elevation	Observed	Target
Aspirin	91%	>90%
Aspirin + clopidogrel	23%	>75%
LMWH and/or UFH	91%	>90%
Beta-blocker (iv/orally)	83%	>75%
GP IIb/IIIa + planned PCI	50%	>75%

patients. Table 3 compares the observed and recommended use of medication in this group of patients. The use of aspirin, heparin and  $\beta$ -blockers is in the expected range, while clopidogrel and glycoprotein IIb/IIIa receptor blockers are underused relative to the guidelines. The checklist in table 2 may assist cardiologists to record management of patients with acute coronary syndromes in their practice.

**Coronary revascularisation**

In patients with acute coronary syndromes, coronary revascularisation is recommended either as direct PCI in patients with evolving myocardial infarction, or in patients without ST elevation at increased risk of death and myocardial infarction. Different risk factors have been identified in guidelines by the European Society of Cardiology as well as the American organisations, including recurrent ischaemia, elevated troponin, haemodynamic instability, major arrhythmia (VT, VF), early post-MI angina and diabetes.

In clinical practice, however, indications for revascularisation are determined as much by availability (in hospitals with, versus those without facilities for PCI and cardiac surgery) as by risk assessment.



*Figure 3. Proportion of patients receiving antithrombotic,  $\beta$ -blocker or statin therapy for secondary prevention. Hospitals are ranked from left to right from low to high use of medication. Note important variation in the use of  $\beta$ -blockers and statins.*

**Table 5.** Checklist lifestyle factors at discharge.

Stop smoking	Done?	If no, why not:
Advice smoking cessation	Y / N	.....
Additional practical material	Y / N	.....
Advice smoking cessation intervention or multifactorial programme	Y / N	.....
Nicotine replacement therapy	Y / N	.....
Follow-up visit planned	Y / N	.....

After the BARI (Bypass Angioplasty Revascularisation Investigation) trial, CABG was recommended and PCI was discouraged in patients with diabetes. Indeed, in BARI, patients with diabetes had an excess mortality after PCI compared with CABG.<sup>5</sup> However, the use of stents and new pharmacological interventions may improve outcome of PCI in diabetes. Indeed, other studies such as ARTS (Arterial Revascularisation Therapy Study), did not confirm these observations.<sup>6</sup> In clinical practice, the proportion of patients with and without diabetes referred for PCI or surgery is similar, according to the Euro Heart Survey observations.

In patients undergoing coronary revascularisation for stable angina, or after an acute coronary syndrome, medical therapy should include cholesterol-lowering agents, statins, and in many patients  $\beta$ -blockers. We recommend such drugs in over 90% and over 75% of patients, respectively. Figure 3 presents the proportion of patients discharged with antithrombotic therapy,  $\beta$ -blockers and statins after a revascularisation in the Netherlands. It is apparent that  $\beta$ -blockers and particularly statins are underused!

### Secondary prevention, lifestyle

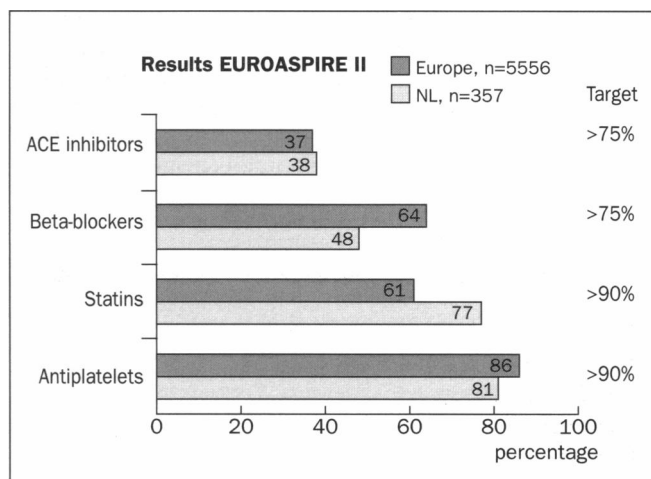
Patients with coronary heart disease or other atherosclerotic diseases should make healthy food choices including a total fat intake  $\leq 30\%$  of total calories, intake of saturated fatty acids and trans fatty acids  $\leq 10\%$  of total fat intake, total cholesterol intake  $< 30$  mg/day and lots of fruits, cereals and vegetables. Furthermore, patients should refrain from smoking. Regular physical exercise is recommended.<sup>7</sup>

Approximately 20% of patients with coronary disease smoke, in spite of the evidence demonstrating that risk for future events can be reduced by about 33% after smoking cessation. Intervention studies clearly demonstrate that intensive programmes, supported by the use of medication, are required to attempt to modify the behaviour of patients who continue to smoke after a cardiovascular event. The creation of such stop smoking programmes throughout the Netherlands is encouraged. At the autumn meeting of the Netherlands Society of Cardiology about 50% of cardiologists indicated that they would be willing to prescribe

nicotine-replacement therapy or other support for patients who wish to stop smoking. Yet, the other half considered this not to be their task. A checklist to record the advice given to patients with coronary disease is presented in table 5.

### Secondary prevention, medical treatment

Current guidelines recommend use of aspirin in all patients with coronary heart disease. Clopidogrel should be prescribed in those patients not tolerating aspirin and in addition to aspirin for nine months in patients after acute coronary syndromes without ST elevation. Beta-blockers are recommended as well as lipid-lowering therapy (statins) if total cholesterol is greater than 4.5 mmol/l (LDL  $\geq 2.5$  mmol/l) in spite of dietary measures. Since the presentation of the guidelines, additional data have been revealed regarding ACE inhibitors. In view of the consistent results from the HOPE (Heart Outcome Prevention Evaluation) and more recently EUROPA (EUROpean trial On reduction of cardiac events with Perindopril in stable cAd) studies, we suggest that ACE inhibitors should be considered in addition to aspirin, statins and  $\beta$ -blockers in all patients with coronary heart disease.<sup>8,9</sup> Figure 4 shows the use of secondary preventive



**Figure 4.** Proportion of patients using ACE inhibitors,  $\beta$ -blockers, statins and antiplatelet therapy in Europe and in the Netherlands (EuroAspire II Survey).

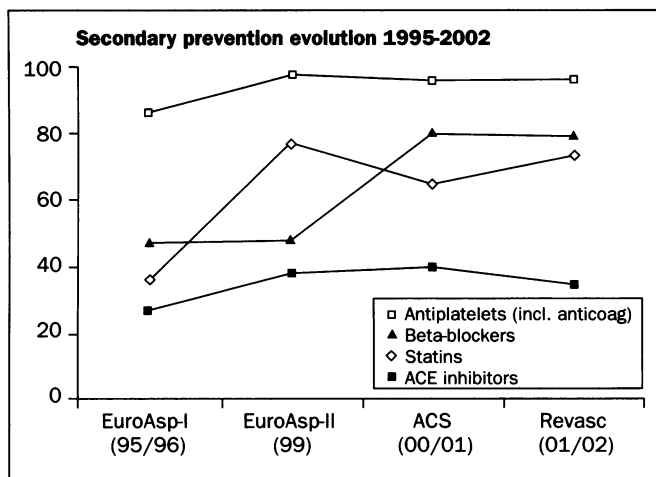


Figure 5. Gradual improvement of therapy for secondary prevention of coronary artery disease from 1995 to 2002. Data are combined from four surveys as indicated.

medication in the 2000 EUROASPIRE II (European Action on Secondary Prevention by Intervention to Reduce Events) study in the Netherlands and in other European countries.<sup>10,11</sup> In the year 2000 the targets were not met for statins, ACE inhibitors and  $\beta$ -blockers. However, a significant improvement was observed over a series of surveys conducted between 1995 and 2002 (figure 5). A checklist to record medical therapy in patients with coronary heart disease is presented in table 6.

### Valvular heart disease

Interventions in patients with valvular heart disease include mechanical prostheses, bioprostheses, homografts, valve repair (in particular for mitral insufficiency) and percutaneous interventions for mitral stenosis. Comparing the actual practice in the Euro Heart Survey programme in 5001 patients with guidelines, it is evident that overall the indications for different types of interventions are compatible with the guidelines.<sup>12</sup>

Endocarditis prophylaxis is recommended in patients with previous endocarditis, in patients with valvular heart disease, including bicuspid aortic valve and mitral prolapse with murmur, and in patients with valve prostheses. In the survey it became apparent that

Table 7. Checklist medical treatment for valvular disease.

Interventions	Prescribed	If no, why not:
Anticoagulation	Y / N	.....
ASA	Y / N	.....
ACE inhibitor	Y / N	.....
Endocarditis prophylaxis	Y / N	.....
Patient education	Y / N	.....

Table 6. Checklist medical therapy for coronary heart disease.

Treatment	Prescribed	If no, why not:
Antithrombotics	Y / N	.....
Beta-blocker	Y / N	.....
Statins	Y / N	.....
ACE inhibitor	Y / N	.....
	Performed	Planned
PCI	Y / N	Y / N
CABG	Y / N	Y / N

between 25 and 40% of patients undergoing dental or other procedures did not receive endocarditis prophylaxis in spite of recommendations.

Anticoagulation is recommended in all patients early after valve surgery. Although not recommended, and not registered for this purpose, low-molecular-weight heparin is used as frequently as unfractionated heparin. In the absence of randomised comparisons of low-molecular-weight heparin and unfractionated heparin, a registry might be created to collect data on efficacy and safety of treatment with low-molecular-weight heparin in patients with valvular disease.

A checklist for medical treatment in patients with valvular disease is presented in table 7.

### Heart failure

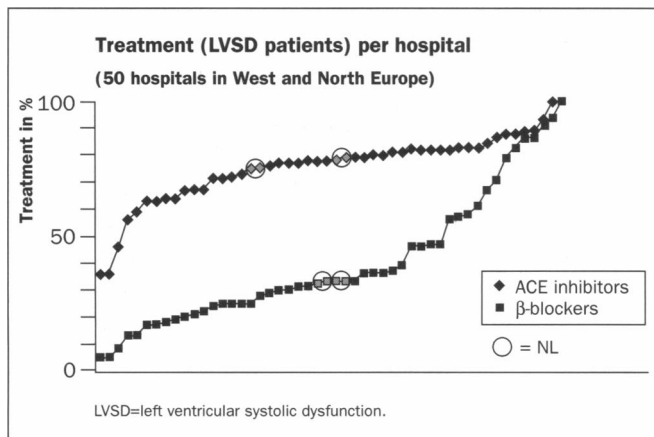
Patients with heart failure and those with asymptomatic left ventricular dysfunction should receive different drugs for prognostic purposes including ACE inhibitors and  $\beta$ -blockers.<sup>13,14</sup> Angiotensin II receptor blockers should be prescribed in patients not tolerating ACE inhibitors. In table 8 the use of ACE inhibitors and  $\beta$ -blockers is presented in 10,701 patients enrolled in the Euro Heart Survey on heart failure, conducted in 2000 and 2001.<sup>15,16</sup>

There is an apparent underuse of both classes of drugs. Furthermore, it is striking that the majority of

Table 8. ACE inhibitor/ $\beta$ -blocker use in EHS-HF.

ACE inhibitors	Observed	Target
Use in patients with LVSD	79%	>90%
≥50% of target dose	51%	>90%
≥100% of target dose	29%	>50%
Beta-blockers		
Use in patients with LVSD	49%	>75%
≥50% of target dose	16%	>90%
≥100% of target dose	4%	>50%

LVSD = left ventricular systolic dysfunction.



**Figure 6.** Proportion of patients with left ventricular systolic dysfunction who receive ACE inhibitor or  $\beta$ -blocker therapy. Presentation as in figure 3. The large open circles represent hospitals from the Netherlands. Note a major variation in use of drug of these recommended drugs among different hospitals.

patients are not treated with the appropriate dose, as tested in clinical trials. For both classes of drugs there is a wide variation in the proportion of patients treated among the different hospitals (figure 6). Management of heart failure, as well as other types of cardiovascular disease, may be improved by systematic verification of chronic treatment using a checklist as presented in table 9.

### Guidelines versus practice

From the Euro Heart Survey/Zorgprogramma it is evident that guidelines are not always applied in cardiology practice. This may be due to different reasons.

First, the physician may not be aware of all aspects of the guidelines, which refer to specific patients. This may be improved by dedicated education programmes (figure 1), as well as by better presentation of the guidelines. The checklists presented in this report may indeed help to remind physicians of the recommended therapy in specific patients. Furthermore, sophisticated computer systems are under development, which aim to present the appropriate sections of guideline upon request, related to the characteristics of each individual patient as seen in the (outpatient) clinic.

Second, the physician may not agree with the guideline recommendations. For example, many cardiologists do not agree with the recommended medication of GPIIb/IIIa blockers in all patients with acute coronary syndromes undergoing PCI, in spite of consistent findings in a series of randomised trials.

Third, the guidelines may not be applicable to certain groups of patients. Indeed, guidelines are often based on 'evidence' from clinical trials, which studied selected patient groups. In particular elderly patients, and patients with multiple concomitant disorders are often excluded from these trials.

**Table 9.** Checklist systematic verification chronic treatment.

Pharmacological treatment [preserved/depressed LVF]	Prescription		If no, why not:
	Y / N		
Antithrombotics	Y / N	.....	
ACE inhibitor/ARB	Y / N	.....	
Beta-blocker	Y / N	.....	
Aldosterone antagonist	Y / N	.....	
Cardiac glycosides	Y / N	.....	
Diuretics	Y / N	.....	
Nitrates	Y / N	.....	
Statins (if CHD)	Y / N	.....	

ARB=angiotensin II-receptor blocker.  
CHD=coronary heart disease.  
LVF=left ventricular function.

Fourth, the physician may judge the recommended therapy not appropriate for a given patient, for example because of other concomitant disease, or intolerance to a combination of drugs.

Fifth, application of guidelines may be hampered by lack of resources, financial or otherwise. For example, in a few European countries statins are reimbursed only in patients with very high cholesterol rates, >8 mmol/l, in spite of the evidence-based recommendations to prescribe these drugs in all patients with coronary disease and a LDL cholesterol >2.5 mmol/l (total cholesterol >4.5 mmol/l). In the Netherlands, primary PCI is not offered to the majority of patients with evolving myocardial infarction (recommended first-choice therapy), because of the restricted capacity of PCI centres. Nevertheless, the proportion of patients offered primary PCI is gradually improving.

Systematic registration of the reasons why physicians deviate from practice guidelines will help to improve the guidelines if needed, and to identify issues which require better education or organisational changes in the local or overall healthcare system. The Euro Heart Survey/Zorgprogramma has been developed for this purpose, while the checklists presented in this report may be of help in your own practice.

### Comments and conclusions

The options for treatment of patients with different types of cardiovascular disease are evolving rapidly. Accordingly, cardiologists and other physicians must continuously review the treatments that they apply in their practice. This applies particularly to treatments prescribed to reduce progression of the disease and improve prognosis. Although patients may question the need for such treatment, and may demand a reduction in the amount of medication, combination treatment with different drugs according to guidelines, at the appropriate dosages as used in clinical trials, should be considered in all patients with coronary heart

disease, valvular heart disease and heart failure. The checklists presented above may assist the physician to optimise patient care.

It is appreciated that recommended treatment might not be appropriate in some patients. It will be particularly useful to document the reasons not to prescribe such modes of therapy, and subsequently discuss the validity of these exceptions.

The Netherlands Society of Cardiology, with support from the Netherlands Heart Foundation, will further develop the checklists presented above, and propose interactive computer programmes, which may remind cardiologists and other physicians of the recommended actions in individual patients, and document their response. In the meantime the quality of the practice of cardiology can be verified in each hospital with the following four steps:

- 1 Review of the guidelines provided by the European Society of Cardiology and Netherlands Society for Cardiology;
- 2 Formulate targets for management of patients in that particular practice, indicating the proportion of patients who should receive a specific therapy, the appropriate dose levels, and for patients with evolving myocardial infarction acceptable time delays for treatment;
- 3 Register your performance by applying the checklists above to a sample of consecutive patients, for example during a four-week period;
- 4 Analyse the results from point 3 and formulate improvements when appropriate. ■

## References

- 1 Werf F van de, Ardissino D, Betriu A, Cokkinos DV, Falk E, Fox KAA, et al. Task Force of the ESC. Management of Acute Myocardial infarction in patients with ST-segment elevation. *Eur Heart J* 2003;24:28-66.
- 2 Hasdai D, Behar S, Wallentin L, Danchin N, Gitt AK, Boersma E, et al. A prospective survey of the characteristics, treatments and outcomes of patients with acute coronary syndromes in Europe and the Mediterranean basin; the Euro Heart Survey of Acute Coronary Syndromes (Euro Heart Survey ASC). *Eur Heart J* 2002;23(15): 1190-201.
- 3 Bertrand ME, Simoons ML, Fox KAA, Wallentin LC, Hamm CW, McFadden E, et al. The Task Force on the management of Acute Coronary Syndromes of the European Society of Cardiology. *Eur Heart J* 2002;23:1809-40.
- 4 The NVVC Working Group Guidelines for the management of patients with non-ST-elevation acute coronary syndromes. *Neth Heart J* 2002;10(2):54-64.
- 5 The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. *N Engl J Med* 1996;335: 217-25.
- 6 Serruys PW, Unger F, Sousa JE, Jatene A, Bonnier HJRM, Schonberger JPAM, et al. For the Arterial Revascularization Therapies Study Group. Comparisons of coronary-artery bypass surgery and stenting for the treatment of multivessel disease. *N Engl J Med* 2001;344(15):1117-24.
- 7 Backer G de, Ambrosioni E, Borch-Johnson K, Brotons C, Cifkova R, Dallongeville J, et al. Third Joint Task Force of European and other Societies on Cardiovascular Disease Prevention in Clinical Practice. *Eur Heart J* 2003;24:1601-10.
- 8 The Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000; 342:145-53.
- 9 The EUROPA Investigators. EUROpean trial On reduction of cardiovascular events among patients with stable coronary artery disease: a randomised, double-blind, placebo-controlled, multicentre trial (EUROPA study). *Lancet* 2003;362:782-8.
- 10 EUROASPIRE II Study Group. Lifestyle and risk factor management and use of drug therapies in coronary patients from 15 countries. Principle results from EUROASPIRE II Euro Heart Survey Programme. *Eur Heart J* 2001;22: 554-72.
- 11 Deckers JW, Jansen C, Scholte op Reimer WJM, Boersma H, Veerhoek MJ, Vos J. Cardiovasculaire risicofactoren bij patienten behandeld wegens coronaire hartziekte: toegenomen medicatiegebruik in de regio Rijnmond in 1999 met 1995/96. *Ned Tijdschr Geneesk* 2001;145 (25):1209-13.
- 12 Iung B, Baron G, Butchart EG, Delahaye F, Gohlke-Bärwolf C, Levang OW, et al. A prospective survey of patients with valvular heart disease in Europe: The Euro Heart Survey on Valvular Heart Disease. *Eur Heart J* 2003;24:1231-43.
- 13 Working Group on Heart Failure of the European Society of Cardiology. *Eur Heart J* 1997;18:736-53.
- 14 Remme WJ, Swedberg K. Guidelines for the diagnosis and treatment of chronic heart failure. *Eur Heart J* 2001;22:1527-60.
- 15 Cleland JGF, Swedberg K, Follath F, Komajda M, Cohen-Solal A, Aguilar JC, et al. The Euro Heart Survey programme – a survey on the quality of care among patients with heart failure in Europe: Part 1: patient characteristics and diagnosis. *Eur Heart J* 2003;24: 442-63.
- 16 Komajda M, Follath F, Swedberg K, Cleland J, Aguilar JC, Cohen-Solal A, Dietz R, Gavazzi A, van Gilst WH. The Euro Heart Failure Survey programme – a survey on the quality of care among patients with heart failure in Europe: Part 2: treatment. *Eur Heart J* 2003; 24:464-74.